UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

Date: April 3, 2009

MEMORANDUM

SUBJECT: **Alkyl Amine Polyalkoxylates (JITF CST 4 Inert Ingredients).** Human Health Risk Assessment to Support Proposed Exemption from the Requirement of a Tolerance When Used as Inert Ingredients in Pesticide Formulations.

PC Code: 790402
Decision No.: 389251
Petition No.: 8E7382
Risk Assessment Type: Single Chemical Aggregate
TXR No.: NA
MRID No.: 46902001,46902005, 46902007, 46914604, 46918001, 46918002, 46918003, 46918004, 46930503, 47041301, 47041302, 47066302, 47097401, 47193901, 47405101

DP Barcode: D360944
Registration No.: NA
Regulatory Action: Inert Tolerance Exemption
Case No.: NA
CAS No.: 61791-26-2, 61791-31-9, 70955-14-5, 68213-26-3
40 CFR: 180.920, 180.930

FROM: Donna S. Davis, Risk Assessor, RAB VII
Alexandra LaMay, Biologist, RAB VII
Matthew Lloyd, Industrial Hygienist, RAB VII
Christine L. Olinger, Chemist, RAB VII
Sheila Piper, Dietary Exposure Assessor, RAB VI
Deborah Smegal, Toxicologist, RAB VII
Linda Taylor, Toxicologist, RAB VII
Health Effects Division (7509P)

THROUGH: Michael S. Metzger, Chief
Risk Assessment Branch VII
Health Effects Division (7509P)

TO: Kerry Leifer, Team Leader
PV Shah, Chief
Inert Ingredient Assessment Branch
Registration Division (7505P)

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1.0 Executive Summary

The Joint Inert Task Force (JITF) Cluster Support Team Number 4 (CST4) has submitted a petition proposing to establish exemptions from the requirement of a tolerance for the following clusters of compounds when used as inert ingredients in pesticide formulations.

> N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl) C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl) content is 2 – 60 moles.
>
> N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl) C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl) content is 2 – 60 moles.

The compounds, referred to as alkyl amine polyalkoxylates (AAPs), are not discrete compounds, but are a mixture of compounds formed from the reaction of fatty acid derived amines with either ethylene oxide or propylene oxide. The AAPs are used primarily as surfactants in pesticide formulations. The petitioner is proposing to limit the maximum amount of the inert in any end-use product to no more than 10% in fungicide and insecticide products and no more than 25% in herbicide formulations.

The toxicology database is adequate to support the use of the alkyl amine polyalkoxylates when used as inert ingredients. The AAPs are not acutely toxic by the oral and dermal routes of exposure, or via inhalation under normal use conditions. Concentrated materials are generally corrosive, eye and skin irritants and may be dermal sensitizers. There is no evidence that the AAPs are neurotoxic, mutagenic, or clastogenic.

There is no clear target organ identified across the AAPs. Following subchronic exposure to rats, some gastrointestinal irritation was observed, but no specific target organ toxicity or neurotoxicity was seen. In subchronic studies in rats and/or dogs, the most sensitive effects noted were increased mortality, clinical signs (salivation, wheezing, emesis, and/or soft feces), cataracts, cellular changes in the stomach, and liver effects characterized by enzyme induction, and pigment accumulation in Kupffer cells and bile canaliculi. There was no increased susceptibility to the offspring of rats following *in utero* exposure in two prenatal developmental toxicity studies. However, there is evidence of increased susceptibility in a reproductive screening study in rats. The points of departure (PoDs) selected for the dietary assessments are lower than the doses at which offspring toxicity occurred in the rat reproduction study and are protective of offspring toxicity occurring at higher doses. There were no residual concerns and the Food Quality Protection Act (FQPA) safety factor was reduced to 1X.

Sufficient data were provided on the chemical identify of the AAPs, however, limited data are available on the metabolism and environmental degradation of the AAPs; further, no residue data were provided. The Agency relied collectively on information provided on the representative chemical structures, the generic cluster structures, the submitted physicochemical EPI Suite™ data, structure-activity relationship information,

as well as information on other surfactants and chemicals of similar size and functionality to determine the residues of concern for this group of inert ingredients. In the absence of data, the Agency has developed an approach that uses surrogate information to derive upper bound exposure estimates for the subject inert ingredients. Acute and chronic dietary risk assessments, which assumed no more than 10% AAP in the final formulation for fungicides and insecticides and 25% for herbicides, resulted in dietary risks that were not of concern.

The Agency evaluated residential handler and post application risks for high-end residential exposure scenarios. The combined margins of exposure (MOEs) for all the residential handler scenarios were above 100, and therefore, did not demonstrate a risk of concern to the Agency.

Short-term and intermediate-term aggregate risks, which combined high end residential exposure with average food and drinking water exposures, were not of concern. Acute and long-term (chronic) aggregate risks that included food and water only, were not of concern.

HED has completed an occupational exposure and risk assessment for the AAPs. Since they can be used in a wide range of applications, HED has selected scenarios that are likely to result in high-end exposure. HED traditionally considers a level of concern (LOC) for these risk assessments to be for an MOE of 100 based on the standard 10x inter and 10x intra species extrapolation safety factors. However, HED notes that for the AAPs, the primary toxic effect seen is related to the surfactants inherent function to disrupt cell membranes resulting in irritating properties to tissues. Given that HED does not expect to see a significant difference between species for this type of effect, an LOC lower than 100 may be appropriate for the non-dietary risk assessments.

Occupational handler risks are not of concern for all scenarios except for workers using a low pressure handwand applying pesticides containing the AAPs to ornamentals in greenhouse settings. HED notes that the occupational handler assessment assumes that mixer/loader/applicators who are handling pesticides containing the AAPs for aerial and ground application on high acreage crops or turf will wear chemical-resistant gloves. HED believes this is a reasonable assumption given the volume of pesticide handled for these applications. Since MOEs for workers applying pesticides to ornamentals in greenhouses containing the AAPs in herbicides at 25%, the requested maximum allowable amount, and in herbicides and insecticides at 10%, do not exceed 100, HED has provided additional exposure and risk estimates reflecting lower percentages in final formulations. HED has provided risk estimates in this document for workers applying pesticides containing AAPs using a low pressure handwand to ornamentals in a green house setting assuming variable amounts of the AAP in herbicide formulations including 25%, 20%, 15%, 10% and 5%. For the insecticide and fungicide assessments, HED has provided estimates assuming variable amounts of the AAP in the formulations including 8%, 6% and 5%.

Occupational post application handler risks exceed an MOE of 100 on the day of

application for all scenarios except for postapplication activities involving herbicides and insecticides on corn, specifically the hand-harvesting / detassling scenario. Those scenarios resulted in MOE of 26 and 69, respectively on the day of application (Day 0). The Agency notes that it is not expected to be typical agricultural practice to apply herbicides or insecticides on the same day workers would be conducting hand harvesting and detassling activities.

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf).

This assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide. These studies have received the appropriate ethical review for use in risk assessment.

Regulatory Recommendation

There are no human health exposure or risk issues that would preclude the approval of an exemption from the requirement of a tolerance for the inert ingredients generically referred to as alkyl amine polyalkoxylates (AAPs), provided the following limitations are addressed specifically in the exemption statement:

- The maximum percent by weight of the AAPs in fungicide and insecticide products should be limited to no more than 10% with the one exception noted below.
- The maximum percent by weight of the AAPs in herbicide formulations should be limited to no more than 25%, with the one exception noted below.
- The maximum percent by weight of the AAPs in herbicide, fungicide and insecticide formulations intended for application by low pressure handwands to ornamentals in a green house setting may need to be reduced from the petitioner requested caps based on a risk benefit assessment for this scenario.
- HED assumed no indoor uses exist. This should be validated by RD, and restrictions on use of these inerts for indoor-use products should be mandated.

HED has no objection to the expansion of this exemption to include not only AAPs derived from animal and plant sources, but also from AAPs derived from petrochemical sources. The specific limitations noted above should be applied to the two cluster classifications that the petitioner has proposed:

> N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl) C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl) content is 2 – 60 moles

N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl) C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl) content is 2 – 60 moles

2.0 Background

Inert ingredients are those ingredients that are added to end use products that are not active ingredients. The terms "active ingredient" and "inert ingredient" are defined under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). An active ingredient is one that prevents, destroys, repels or mitigates a pest, or is a plant regulator, defoliant, desiccant or nitrogen stabilizer. The statute defines the term "inert ingredient" as an ingredient that is not active.

As mandated by the Food Quality Protection Act (FQPA) of 1996, EPA conducted a reassessment of inert ingredients used in pesticide products to determine if they met the Agency's current standard of safety. As a result of that reassessment, the Agency published a final rule in the Federal Register (FR Notice Volume 71, No. 153, p. 45422) proposing revocation of specific exemptions from the requirement of a tolerance due to insufficient data. These tolerance exemptions are currently slated to be revoked on August 9, 2009 and included the following exemptions:

180.920 m. N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxyethylene) alkylamine; the poly(oxyethylene) content averages 3 moles; the alkyl groups (C14-C18) are derived from tallow, or from soybean or cottonseed oil acids.

180.920 n. N,N-Bis (2-hydroxyethyl)alkylamine, where the alkyl groups (C8 – C18) are derived from coconut, cottonseed, soya, or tallow acids.

180.920 o. N,N-Bis 2-([omega]-hydroxypolyoxyethylene) ethyl) alkylamine; the reaction product of 1 mole N,N-bis(2-hydroxyethyl)alkylamine and 3-60 moles of ethylene oxide, where the alkyl group (C8-C18) is derived from coconut, cottonseed, soya or tallow acids.

180.920 p. N,N-Bis 2-([omega]-hydroxypolyoxyethylene/polyoxypropylene) ethyl) alkylamine; the reaction product of 1 mole N,N-bis(2-hydroxyethyl)alkylamine and 3-60 moles of ethylene oxide and propylene oxide, where the alkyl group (C8-C18) is derived from coconut, cottonseed, soya or tallow acids.

The Joint Inert Task Force (JITF) Cluster Support Team Number 4 (CST4) has submitted Petition #8E7382, proposing to consolidate and replace the four exemptions listed above with exemptions for the JITF CST4 inert ingredients known collectively as alkyl amine polyalkoxylates or "AAPs". The JITF CST4 is proposing to establish the following tolerance exemptions:

N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl) C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl) content is 2 – 60 moles.

N,N-Bis-[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl) C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl) content is 2 – 60 moles.

HED notes that while the proposed exemptions do represent a consolidation of the four exemptions slated for revocation, they also expand the previously approved exemptions to include alky amine polyalkoxylates manufactured from the reaction of ethylene oxide and propylene oxide with fatty acids derived from not only animal and plant sources, but also from petrochemical sources.

3.0 Ingredient Profile

3.1 Summary of Proposed Uses

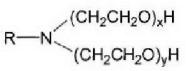
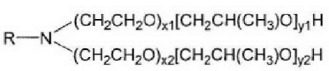
Alkyl amine polyalkoxylates are used primarily as surfactants in pesticide formulations. Additionally, the petitioner notes that these mixtures may also be used to a lesser extent as emulsifiers and wetting agents. While the AAPs are inert ingredients in all classes of pesticides, the majority of use reported by the petitioner is in herbicide and fungicide products. The petitioner indicates that currently the concentration of AAPs in formulated products generally does not exceed 25% by weight.

The petitioner is proposing to limit the use of AAPs in herbicide formulations to no more than 25% by weight and 10% by weight in all other pesticide formulations.

In addition to uses as inerts in pesticide formulations, AAPs have a variety of industrial applications. They appear to have very limited use in consumer or personal care products and the petitioner states that concentrations in potential consumer care products would be at lower concentrations than proposed in pesticide formulations.

3.2 Structural Information

The "alkyl amine polyalkoxylates" refers not to a discrete compound, but to mixtures of compounds. Information on the generic structures of these compounds and the manufacturing process to derive these surfactants is summarized in Table 3.2, below.

TABLE 3.2. Alky Amine Polyalkoxylate (AAP) Chemical Information	
Chemical Structure	These surfactants are typically complex mixtures formed from the reaction of fatty acid derived amines with either ethylene oxide or propylene oxide. The AAP carbon chain is defined in the exemption request as ranging from C8 – C18. The degree of polyalkoxylation is defined in the range of 2 to 60 moles. The generic structures for the alkylamine polyethoxylated compounds (AAP, POE) and alkylamine polypropoxylated (AAP POP) compounds are shown below.[1] **Figure 1a. Generic AAP POE Structure:** § 180.920: N,N-Bis-[[alpha]-ethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl)] C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl) content is 2-60 moles.  R = Alkyl C8-18, linear or branched, saturated or unsaturated; Average x + y = 2-60 moles; x, y ≠ 0 **Figure 1b. Generic AAP POE/POP Structure:** § 180.920: N,N-Bis-[[alpha]-ethyl/methylethyl-[omega]-hydroxypoly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl))] C8-C18 saturated and unsaturated alkylamines; the poly(oxy-1,2-ethanediyl/oxy(methyl-1,2-ethanediyl)) content is 2-60 moles.  R = Alkyl C8-18, linear or branched, saturated or unsaturated; Average x1 + x2 + y1 + y2 = 2-60 moles; x1, x2, y1, y2 ≠ 0
Common name	Alkyl Amine Polyethoxylates (AAPs)
Use Class	Non ionic surfactants used as inert ingredients in pesticide formulations. May also be used as emulsifiers and wetting agents.
Discussion of Synthesis	AAPs are synthesized by reacting fatty acids or petrochemical derived long carbon chain acids with ammonia at high temperatures to generate long chain fatty acid type carbon amides which are dehydrated to the nitrile and then reduced to a primary fatty acid derived amine. The amine is then reacted with ethyl oxide or ethylene oxide and propylene oxide to form tertiary amine polyalkoxylates (POE or POE/POP). The alkyl amine precursors can be from plants, animals or petrochemicals.[2] The registrant has indicated (personal communication to K. Leifer) that branching consists of methyl groups and not longer branched chains.

[1] Figure 1a and 1b excerpted directly from petition, page 8 dated June 19, 2008.

[2] Manufacturing process description taken from petition, page 11 dated June 19, 2008.

3.3 Physical and Chemical Properties

As noted previously, the AAPs are not discrete chemicals, but are complex mixtures of chemicals. To address the requirement to provide information on physical and chemical properties, the registrant selected four representative compounds and modeled physicochemical data using EPI Suite™ modeling (http://www.epa.gov/opptintr/expsoure/pubs/episuite.htm). Results of the EPI Suite™ modeling as reported by the registrant are summarized in Table 3.3, below.

Table 3.3. Physicochemical Properties of Representative Alky Amine Polyalkoxylates[1]						
CAS No. (Company Name)	**Molecular Formula (MW)**	**Log K_{OW}**	**Water Solubility (mg/L)**	**Henry's Law Constant**	**Melting Point (°C)**	**Vapor Pressure (mm Hg @ 25 °C)**
61791-26-2	$C_{48}H_{97}NO_{15}$ (928.31)	3.15	381.83	4.2×10^{-33}	349.84	5.8×10^{-27}
61791-31-9 (MON 8109)	$C_{16}H_{35}NO_2$ (273.46)	3.90	299.47	1.94×10^{-9}	131.43	1.76×10^{-8}
70955-14-5	$C_{18}H_{39}NO_2$ (301.52)	4.96	19.48	4.99×10^{-10}	127.14	3.86×10^{-8}
68213-26-3 (Armoblend 557)	$C_{64}H_{129}NO_{17}$ (1184.74)	7.53	6.685×10^{-8}	2.37×10^{-34}	349.84	3.77×10^{-33}

[1] Table values taken directly from submission entitled *Petition Proposing an Exemption from the Requirement of a Tolerance for Residues of Joint Inerts Task Force Cluster 4 "Alkyl Amines Polyalkoxylates" in or on Raw Agricultural Products and Food Products.* Submitted by JITF Cluster Support Team Number 4, 6/19/2008, Table 7, pp 19 – 20.

4.0 Hazard Characterization/Assessment

4.1 Hazard and Dose-Response Characterization

4.1.1 Database Summary

The available mammalian toxicology database includes acute, subchronic repeat dose oral, developmental, reproductive, and mutagenicity data for four representative compounds of the alkyl amine polyalkoxylate (AAP) group. The toxic effects seen in the submitted studies include gastrointestinal problems due to local irritation and corrosive effects. The chemicals for which toxicity data were submitted are listed below:

►**MON 0818 [CAS 61791-26-2 (tallow); Ave POE n=15]** acute oral and dermal, eye and skin irritation, dermal sensitization, Ames, *in vivo* mouse micronucleus assay, 4-week rat (diet), 3-month rat (diet), **OECD 421** 2-generation reproduction rat screening (diet), **OECD 422** 28-day rat reproductive/developmental (diet);

►**MON 8109 [CAS 61791-31-9 (coco); Ave POE n=2]** acute oral and inhalation, eye and skin irritation studies, **OECD 422** 28-day rat repeated oral dose (dietary) reproductive/developmental;

►**ATMER® 163 [CAS 70955-14-5; C13-C15; ave POE n=2]** acute oral, skin irritation, Ames, *in* vitro human peripheral lymphocyte cytogenic assay, *in* vitro mouse lymphoma mutation assay, 90 day rat oral (gavage), 90-day dog (capsule).

►**Armoblen 557 [CAS 68213-26-3; Ave POE n=5/Ave POP n=12]** acute oral and inhalation, eye and skin irritation, Ames, 28-day rat oral (gavage)

The available toxicology data are adequate to support the requested exemption from the requirement of tolerance when used in pesticide formulations for these AAP inert compounds. In a joint meeting of the HED ToxSAC (Toxicology Science Advisory Committee) and the ROCKS (Residues of Concern Knowledge-based Subcommittee), the Agency concluded that the four surrogate chemicals (MON 0818, MON 8109, Atmer 163, and Armoblen 557) are representative of all the chemicals in the AAP cluster. Further, the ToxSAC members agreed that the currently available toxicity dataset is adequate to apply to the cluster and to characterize the potential toxic effects of these surfactants. The ROCKS members noted that there was sufficient bracketing of the range of molecular weights to represent the entire class of AAPs.

The available mammalian toxicity database includes acute, subchronic, developmental, reproductive toxicity studies *via* the oral route as well as mutagenicity data for the four compounds. While there is no chronic toxicity study, the ToxSAC noted that the effects do not increase in severity over time (4 weeks to 13 weeks). Based on the lack of progression of severity of effects with time along with the considerable similarities of effects across the species tested and the observation that the vast majority of the effects observed were related to local irritation and corrosive effects, the ToxSAC concluded that chronic studies would not be required. Moreover, an additional uncertainty factor (UF) for extrapolation from subchronic toxicity study to a chronic exposure scenario would not be needed since the severity of effects did not increase with time and similar effects (related to local irritation) occurred at comparable dose levels across species. As a result, the committee concluded that the typical 100-fold uncertainty factor (10X interspecies and 10X intraspecies) would be adequately protective. The ToxSAC noted that use of the full 10X interspecies factor will actually provide an additional margin of safety because it is not expected that humans' response to local irritation/corrosiveness effects would be markedly different from animals.

4.1.2 Toxicological Effects and Metabolism

Toxicological Effects
As previously noted, the AAPs in this inert class cover the range of C8-C18 carbon lengths and polyalkoxylation of n = 2-60. The majority of toxicology information is available for four AAPs, which is meant to represent the entire class of compounds. Details can be found in the JIFT Cluster Support Team Number 4 (2008) submission.

Generally, lower molecular weight AAPs (lower carbon chain units and less alkoxylation) may potentially be more bioavailable because they may be more easily absorbed and distributed than higher molecular weight compounds. Thus overall, the longer chain carbon amine higher polyalkoxylates should be less bioavailable.
The AAPs are not acutely toxic by the oral and dermal routes of exposure, or via inhalation under normal use conditions (i.e., maximum 25% in pesticide end-use products and non-respirable droplet sizes). Concentrated materials are generally corrosive, eye and skin irritants and may be dermal sensitizers. There is no evidence that the AAPs are mutagenic, or clastogenic.

There is no clear target organ identified across the AAPs. Following subchronic exposure to rats, some gastrointestinal irritation was observed, but no specific target organ toxicity or neurotoxicity was seen. No effects were detected in a functional observational battery (FOB) or motor activity assessment. In a subchronic rat study, the most sensitive effects noted were increased mortality, salivation, wheezing, cataracts, and micro- and macroscopic changes in the non-glandular stomach at doses as low as 30 mg/kg/day. In a subchronic dog study, the most sensitive effects included clinical signs (increased incidence of salivation, emesis, and soft feces) and liver effects characterized by enzyme induction, and pigment accumulation in Kupffer cells and bile canaliculi.

In rat developmental studies, no adverse fetal effects were seen, even at maternally toxic doses. No effects were observed on estrous cyclicity, spermatogenic endpoints, or testosterone and thyroid levels in a two-generation rat reproduction study. However, reproductive and offspring toxicity were noted for AAPs (specifically MON 0818 and MON 8109) based on litter loss, increase mean number of unaccounted-for implantation sites and decreased mean number of pups born, live litter size and postnatal survival from birth to LD 4.

Surfactants are surface-active materials that can damage the structural integrity of cellular membranes at high dose levels. Thus, surfactants are often corrosive and irritating in concentrated solutions, as indicated by the acute toxicity studies for these inert materials. It is possible that some of the observed toxicity seen in the repeated studies, such as diarrhea or decreased body weight gain, can be attributed to the corrosive and irritating nature of these surfactants.

Metabolism
Very little metabolism information is available for the alkyl amine polyalkoxylates. However, it is possible to predict mammalian metabolism based on studies for the alkyl alcohol alkoxylates, which are another class of surfactants. It has been proposed that the primary metabolic pathway involves the excretion of the polyalkoxylate moiety and conversion of the alkyl amine group to a fatty acid that is then converted via oxidative degradation to carbon dioxide and water.

In general, the gastrointestinal absorption of AAPs with relatively short alkoxylate chain lengths is expected to be rapid and extensive, while less absorption is likely for the more extensively polyalkoxylated AAPs with larger molecular weights.

4.2 Dose Response Assessment

The Agency believes the dose-response assessment described herein and used for risk assessment purposes for the AAPs is conservative because the most health protective surrogate chemical was selected to represent the entire AAP class of inert ingredients.

4.2.1 Acute Reference Dose (aRfD) – All Populations

Study Selected: developmental toxicity – rat (OPPTS 870.3700)
MRID No.: 46902005
Executive Summary: See Appendix A, Guideline §870.3700

Dose and Endpoint for Risk Assessment: NOAEL = 72 mg/kg/day, based on 2 deaths on gestation day (GD) 8 (after 2 doses) at the LOAEL of 216 mg/kg/day.
Uncertainty Factor(s): 100X (10 interspecies; 10X intraspecies)

Comments about Study/Endpoint/Uncertainty Factors: The rats in this study were administered a test material that contained 71.9% of the inert ingredient to be tested, therefore the doses in this study were adjusted accordingly. The executive summary for the rat developmental toxicity study may be found in Appendix A, Section A.3 of this document.

4.2.2 Chronic Reference Dose (cRfD)

Study Selected: 90-day oral toxicity – rat (OPPTS 870.3100)
MRID No.: 47041301
Executive Summary: See Appendix A, Guideline §870.3100

Dose and Endpoint for Risk Assessment: NOAEL = 15 mg/kg/day, based on increased mortality, salivation, and posterior subcapsular cataracts in males as well as wheezing, and micro- and macro-scopic changes in the non-glandular stomach of both sexes at the systemic LOAEL of 30 mg/kg/day.
Uncertainty Factor(s): 100X (10 interspecies; 10X intraspecies)

Comments about Study/Endpoint/Uncertainty Factors: The purity of the test material was not reported in the study, but the Agency confirmed via personal communication that this inert ingredient (ATMER 163) is a nominally 100% pure product. The study provides the lowest NOAEL. Two deaths occurred at 30 mg/kg/day (on days 36 and 78). Although the duration of exposure was 90 days, there is no need for an additional uncertainty factor because the effects do not seem to increase in severity over time (4 weeks to 13 weeks). Based on the lack of progression of severity of effects with time along with the considerable similarities of effects across the species tested and the observation that the vast majority of the effects observed were related to local irritation and corrosive effects, the ToxSAC concluded that an additional UF for extrapolation from subchronic toxicity study to a chronic exposure scenario would not be needed. As a result, the ToxSAC concluded that the typical 100-fold uncertainty factor would be sufficiently protective since it is not expected that humans' response to local irritation/corrosiveness effects would be markedly different from animals. The executive summary of the subchronic oral toxicity study in rats may be found in Appendix A, Section A.3 of this document.

4.2.3 Incidental Oral (Short-Term and Intermediate-Term), Dermal (All Durations) and Inhalation (All Durations)

Study Selected: 90-day oral toxicity – rat (OPPTS 870.3100)
MRID No.: 47041301
Executive Summary: See Appendix A, Guideline §870.3100

Dose and Endpoint for Risk Assessment: NOAEL = 15 mg/kg/day, based on increased mortality, salivation, and posterior subcapsular cataracts in males as well as wheezing, and micro- and macroscopic changes in the non-glandular stomach of both sexes at the systemic LOAEL of 30 mg/kg/day.
Uncertainty Factor(s): 100X (10 interspecies; 10X intraspecies)

Comments about Study/Endpoint/Uncertainty Factors: The study provides the lowest NOAEL. Two deaths occurred at 30 mg/kg/day (days 36 and 78). Although the duration of exposure was 90 days, there is no need for an additional uncertainty factor for risk assessments reflecting longer exposure durations because the effects do not seem to increase in severity over time (4 weeks to 13 weeks). The executive summary of the subchronic oral toxicity study in rats may be found in Appendix A, Section A.3 of this document. A dermal absorption factor of 5% is recommended (see section 4.2.5). Since no inhalation absorption data are available for the surrogate chemicals, toxicity by the inhalation route was considered to be equivalent to toxicity by the oral route of exposure.

4.2.4 Dermal Absorption

There are no dermal absorption data on the AAPs. However, data on functionally and structurally similar surfactants suggest that dermal absorption of the AAPs is likely to be low. As referenced in Section B of the petition (JITF CST 4 2008), dermal absorption models commonly used in the cosmetic and detergent industries also suggest low systemic exposure for AAPs. Predicted dermal absorptions for the representative AAP chemicals using such models were said to range from negligible to 1.1% absorption. Based on the lack of data for the AAPs and the irritant properties of these surfactants, in order to be health protective, a conservative dermal absorption factor of 5% was selected.

4.3 FQPA Considerations

The toxicity database, with respect to FQPA, consists of a rat developmental study (MON 0818) and one rat reproduction study (MON 0818) to cover the C8-C18 (coco and tallow) range of carbon chain length and polyalkoxylation from the lower, more bioavailable end n=2 to the higher end n=15. A summary of these studies is in Appendix A. There are no neurotoxicity studies available for the AAPs; however, there is no indication of neurotoxicity in the available toxicity studies.

HED performed a Degree of Concern Analysis because the rat reproduction study provided evidence of increased susceptibility in the offspring relative to the parents. The purpose of the Degree of Concern analysis was (1) to determine the level of concern for

the effects observed when considered in the context of all available toxicity data; and (2) identify any residual uncertainties after establishing toxicity endpoints and traditional uncertainty factors to be used in the risk assessment.

In the case of the AAPs, there was no increased susceptibility to the offspring of rats following *in utero* exposure in the prenatal development toxicity study. However, there was evidence of increased susceptibility in the reproduction toxicity studies in rats. Offspring effects include litter loss, increased mean number of unaccounted-for implantation sites and decreased mean number of pups born, live litter size and postnatal survival from birth to LD 4 (F1) at 1000 ppm MON 0818 (41-48.6 mg/kg/day) and at 2000 ppm MON 8109 (134-148 mg/kg/day). However, the rat reproduction study identified a NOAEL of 300 ppm for both MON 0818 and MON 8109 (12-14 mg/kg/day and 23-26 mg/kg/day, respectively) for offspring effects, and the selected point of departure for the dietary, dermal and inhalation risk assessments is protective of these offspring effects, thus there are no residual concerns.

There are no residual uncertainties identified in the exposure databases. The food exposure assessments are considered to be conservative. The food and drinking water assessment is not likely to underestimate exposure to any subpopulation, including those comprised of infants and children.

The FQPA factor can be reduced to 1X. A 1X FQPA Safety Factor is appropriate for the following reasons:

- The toxicology database is adequate for assessing the sensitivity of infants and children to AAP exposure.
- No quantitative or qualitative increased susceptibility was demonstrated in the fetuses in the prenatal developmental toxicity study in rats following *in utero* exposure.
- Although there is some increased susceptibility in the rat reproductive toxicity study (where the offspring NOAEL of 300 ppm (12-14 mg/kg/day) was lower than the paternal NOAEL of 1000 ppm (41-48.6 mg/kg/day), the dose-response for this effect has been adequately characterized, and the point of departure for the chronic dietary, dermal and inhalation risk assessment which is based on a NOAEL of 15 mg/kg/day with a 100X uncertainty factor, is protective of the adverse offspring effects.
- Residue values used in the dietary risk assessment are unlikely to underestimate risk.

4.4 Classification of Carcinogenic Potential

There is no evidence that the AAPs are carcinogenic. The Agency used a qualitative structure activity relationship (SAR) database, DEREK11, to determine if there were structural alerts for a representative large molecule, as well as a smaller molecule that had been extensively dealkylated, with the amine group intact. No structural alerts were identified. In addition, there was little concern by the Residues of Concern Knowledge-based Subcommittee (ROCKS) about any of the postulated metabolites having greater

toxicity than the parent compounds. See Appendix B for a complete description of the SAR analysis conducted for the alkyl amine polyalkoxylates.

4.5 Hazard Identification and Toxicity Endpoint Selection

A summary of the points of departure selected may be found in Table 4.5. Points of Departure for risk assessment were selected at a Joint ToxSAC/ROCKS meeting and are documented in the meeting minutes entitled "CST4 Inerts – Joint ToxSAC/ROCKS Meeting on December 9, 2008" (J. Kidwell, 1/16/2009).

The level of concern (LOC) is for MOEs which are less than 100 and is based on 10X for interspecies extrapolation from animals to humans and 10X for variation in sensitivity between humans. These LOCs are applicable to all populations, including individuals exposed in a residential setting and occupationally exposed workers.

An aggregate risk assessment can be performed for the AAPs since common endpoints were selected for the oral, dermal and inhalation routes of exposure.

Table 4.5. Summary of Toxicological Doses and Endpoints for AAPs for Use in Dietary, Non-Occupational, and Occupational Human Health Risk Assessments

Exposure/ Scenario	Point of Departure	Uncertainty Factors	RfD, PAD, Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (all populations)	NOAEL = 72 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 1x	aRfD = aPAD= 0.72 mg/kg/day	**90-day oral toxicity study – rat** MON 0818 [CAS 61791-26-2 (tallow); Ave POE n=15] LOAEL = 216 mg/kg/day, based on mortality (2 deaths after 2 exposures; GD 2), with a total of 6/25 deaths during GD 6-15.
Chronic Dietary (All Populations)	NOAEL = 15 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 1x	cRfD =cPAD= 0.15 mg/kg/day	**90-day oral (gavage) toxicity study – rat ATMER®163 (CAS 70955-14-5 (C13-C15, POE n=2)** LOAEL = 30 mg/kg/day, based on increased mortality [2 deaths (days 36, 78)], salivation, and posterior subcapsular cataracts in males as well as wheezing, and macro- and microscopic changes in the nonglandular stomach of both sexes.
Incidental Oral Short-Term (1–30 days) and Intermediate-Term (1-6 months)	NOAEL = 15 mg/kg/day	UF_A= 10x UF_H=10x FQPA SF = 1x	Residential LOC for MOE = 100	**90-day oral (gavage) toxicity study – rat ATMER®163 (CAS 70955-14-5 (C13-C15, POE n=2)** LOAEL = 30 mg/kg/day, based on increased mortality [2 deaths (days 36, 78)], salivation, and posterior subcapsular cataracts in males as well as wheezing, and macro- and microscopic changes in the nonglandular stomach of both sexes.

Table 4.5. Summary of Toxicological Doses and Endpoints for AAPs for Use in Dietary, Non-Occupational, and Occupational Human Health Risk Assessments				
Exposure/ Scenario	**Point of Departure**	**Uncertainty Factors**	**RfD, PAD, Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Dermal and Inhalation (All Durations)	oral NOAEL = 15 mg/kg/day (5% dermal absorption) (inhalation absorption rate = 100%)	UF_A= 10x UF_H=10x FQPA SF = 1x	Residential/ Occupational LOC for MOE = 100	**90-day oral (gavage) toxicity study – rat ATMER®163 (CAS 70955-14-5 (C13-C15, POE n=2)** LOAEL = 30 mg/kg/day, based on increased mortality [2 deaths (days 36, 78)], salivation, and posterior subcapsular cataracts in males as well as wheezing, and macro- and microscopic changes in the nonglandular stomach of both sexes.
Cancer (oral, dermal, inhalation)	Classification: No animal toxicity data available for an assessment; Based on SAR analysis, AAPs are not expected to be carcinogenic.			

Point of Departure (PoD) = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no observed adverse effect level. LOAEL = lowest observed adverse effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. MOE = margin of exposure. LOC = level of concern. N/A = not applicable.

4.6 Endocrine Disruption

EPA is required under the FFDCA, as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following recommendations of its Endocrine Disruptor and Testing Advisory Committee (EDSTAC), EPA determined that there was a scientific basis for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When additional appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, AAPs may be subjected to further screening and/or testing to better characterize effects related to endocrine disruption.

5.0 Dietary Exposure/Risk Characterization

5.1 Residues of Concern

Very limited information is available for the alkyl amine polyalkoxylates with respect to plant and animal metabolism or environmental degradation. The ROCKS Subcommittee

met in a joint meeting with the ToxSAC on December 9, 2008 to determine if the selected representative chemicals from the AAPs were representative of the entire cluster and to discuss residues of concern. The subcommittee considered the representative chemical structures, the generic cluster structures, the submitted physicochemical EPI Suite™ information as well as the structure-activity relationship analysis detailed in Appendix B of this review. Additionally, the ROCKS members considered information on other surfactants and chemicals of similar size and functionality. The committee concluded that the cluster grouping was appropriate and that there were not likely to be degradates of the alky amine polyalkoxylates that were likely to be of greater toxicological concern than the AAPs themselves.

5.2 Drinking Water Residue Profile

No monitoring data or data reflecting the concentration of these inert ingredients in drinking water is available. For the purpose of the screening level dietary risk assessment to support this request for an exemption from the requirement of a tolerance for the AAPs, a value of 100 ppb based on screening level modeling was used for both the acute and chronic dietary risk assessments.

EFED conducted modeling runs on four surrogate inert chemicals using a range of physical chemical properties which bracket those expected in for the AAPs (email from D. Young to M. Metzger dated 1/15/09). EFED selected a North Carolina cotton scenario with an application date of July 1st as the scenario that would likely provide high end drinking water values for use in risk assessment. Percent crop area (PCA) factors were not applied. Simulations were run assuming a rate of 1 lb inert ingredient/A. Since degradation information was not available, three degradation scenarios were investigated: 1) chemically stable in water and soil; 2) a 100-day half-life in water and soil; and 3) a 10-day half life in water and soil. Further, two possible scenarios were investigated, one where all of the inert was applied as a single application, and the second assuming that the inert was applied evenly over a growing season. Modeled acute drinking water values ranged from 0.001 ppb to 41 ppb. Modeled chronic drinking water values ranged from 0.0002 ppb to 19 ppb. Further details of the EFED analysis are contained in Appendix C of this document.

HED considers the value of 100 ppb to be a high end, conservative assumption that is not likely to underestimate drinking water risks.

5.3 Food Residue Profile

No residue data were submitted for the alkyl amine polyalkoxylate inert ingredients. In the absence of data, the Agency has developed an approach which uses surrogate information to derive upper bound exposure estimates for the subject inert ingredients. Upper bound exposure estimates are based on the highest tolerance for a given commodity from a list of 57 high use insecticides (22), herbicides (20), and fungicides (17). The 57 pesticides were selected based on an overall ranking scheme that included consideration of the 1999 data for active ingredients use. All herbicides at greater than 5

million lbs/yr and all fungicides and insecticides at greater than 1 million lbs/yr were included as candidate surrogate chemicals. The 57 pesticide surrogate candidates are listed in Appendix D of this risk assessment.

OPP assumed that the residue level of the inert ingredient would be no higher than the highest tolerance for a given commodity. Implicit in this assumption is that there would be similar rates of degradation between the active and inert ingredient (if any) and that the concentration of inert ingredient in the scenarios leading to these highest of tolerances would be no higher than the concentration of the active ingredient.

To summarize, the Agency believes the assumptions used to estimate dietary exposures lead to a very conservative assessment of dietary risk for the following reasons:

- the highest tolerance level from the surrogate pesticides for every food is used;
- 100% crop treated is assumed for all crops (every food eaten by a person each day has tolerance-level residues);
- many of these high tolerances are based on very short pre-harvest intervals where there is little time for degradation, whereas actual pesticide applications occur throughout the growing season;
- no consideration was given to potential degradation between harvest and consumption (use of tolerance level residues which are typically one to two orders of magnitude higher than actual residues found in monitoring data);
- residue values were assigned to every commodity in DEEM™ with no consideration given to potential reduction in residues from washing or cooking.

Although sufficient information to quantify actual residue levels in food is not available, the compounding of these conservative assumptions will lead to a significant exaggeration of actual exposures. OPP does not believe that this approach underestimates exposure in the absence of residue data.

5.4 Analytical Methodology

Since this request is for an exemption from the requirement of a tolerance, an analytical method for enforcement purposes is not required to support this action.

5.5 Dietary (Food and Water) Exposure and Risk

The model and inputs used for the AAP dietary risk assessment are described briefly below. A complete description of the dietary exposure and risk assessment is provided in the memorandum entitled "Alkyl Amines Polyalkoxylates (Cluster 4): Acute and Chronic Aggregate (Food and Drinking Water) Dietary Exposure and Risk Assessments for the Inerts." (D361707, S. Piper, 2/25/09).

Acute and chronic aggregate dietary (food and drinking water) exposure and risk assessments were conducted using the Dietary Exposure Evaluation Model DEEM-FCID™, Version 2.03 which uses food consumption data from the U.S. Department of

Agriculture's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998.

5.5.1. Acute Dietary Exposure and Risk

A screening level assessment for acute dietary (food and drinking water) exposure assessment was conducted for the alkyl amine polyalkoxylates. In the absence of actual exposure information HED assumed that the residues of the inert ingredients would be no higher than the highest exposure from 57 of the most significant active ingredients. Inherent in this assumption is the supposition that the inert ingredient will be in the final formulation at no higher percentage than the active ingredient (i.e. 50% active, 50% inert). RD has conducted a review of current formulations used in agricultural settings and has found that individual inert ingredients are not present at levels in excess of the active ingredient (personal communication K. Leifer). The highest tolerance level residue for all food forms, including meat, milk, poultry and eggs, default processing factors for dried commodities and 100% percent crop treated (%CT) were used. No monitoring data or data reflecting the concentration of these inert ingredients in drinking water is available. For the purpose of this screening level dietary risk assessment, a value of 100 ppb was used for drinking water residues for both the acute and chronic dietary risk assessments.

The initial screening level acute dietary exposure estimates for food and drinking water, assuming that the inert ingredient would be in the formulation at a level equivalent to the active ingredient (50% active ingredient; 50% AAP), identified potential risks of concern. HED conducted a more refined assessment to reflect the actual use pattern of these inert ingredients in pesticide formulations. The petitioner has indicated that these inerts will not be used at more than 10% by weight in fungicide and insecticide formulations and at no more than 25% in herbicide formulations.

In refining the dietary risk assessment, HED notes that it is the fungicide tolerances which are typically the highest and serve as the basis for the residue value used in the dietary risk assessment. This is consistent with expectation given that fungicides are often applied late in the season and herbicides and insecticides are typically used much earlier in the season, resulting in much lower residues. HED has not yet developed a dietary exposure model for inerts which would allow for inclusion of inert ingredients at different percentages in the final formulation based on class of pesticide. The current model uses predominantly fungicide residues to estimate a high end exposure. HED does not expect that allowing a maximum of 25% in the final formulation for herbicides only will have a significant impact on the dietary exposure. Across the board it appears that selecting the highest fungicide tolerance and correcting for its limitation to 10% by weight as a maximum in the final formulation, results in a higher residue input into the dietary risk assessment than selecting the highest herbicide tolerance and correcting for 25% by weight as a maximum in the final formulation.

This assertion that herbicides at 25% of the final formulation will not significantly impact risk above that resulting from use of fungicides at 10% of the final formulation is

supported by examining the major drivers in the AAP dietary risk assessment. The major drivers for the AAP dietary risk assessment are apples and grapes. For both of these commodities, the highest tolerances were from the fungicide, captan and were 25 ppm in both crops. The highest herbicide tolerance for apples and grapes was from diuron and was 1 ppm for both crops. To calculate the effective residue level to input into the refined assessment, HED has started with the assumption in the screening level that residues of the active ingredient and the inert are equivalent or that at a maximum, the inert is present in the formulation at 50%. Since the petitioner proposes to cap the use of the AAPs in fungicides to 10%, a 5-fold reduction factor is applied to the residue (25 ppm x 0.2 = 5 ppm). The proposed cap for herbicide use is 25%, so the initial residue value can be refined to account for a 2-fold reduction in the residue from the original herbicide tolerance (1 ppm x 0.5 = 0.5 ppm). Even allowing for a higher percent in the final herbicide formulation, the residue value resulting from the fungicide use is significantly higher than that of the herbicide.

Based on the refined dietary risk assessment which allows for a reduction of residues based on a lower percentage in the final formulation, the AAP dietary exposure at the 95th percentile for food and drinking water is 16% of the aPAD for the U.S. population and 44% of the aPAD for children 1-2 yrs old, the most highly exposed population subgroup. The results for all regulated subgroups are shown in Table 5.5.4, below.

5.5.2 Chronic Dietary Exposure and Risk

A conservative screening level assessment was conducted for chronic dietary (food and drinking water) exposure using the highest tolerance level residue for all food forms, including meat, milk, poultry and eggs, default processing factors for dried commodities and 100% CT. In addition, a default concentration of 100 ppb was assumed for inert ingredient residues in drinking water.

The chronic dietary exposure estimates for food and drinking water, assuming that the inert ingredient would be in the formulation at a level equivalent to the active ingredient, resulted in a screening level assessment which identified potential risks of concern. Based on the results of the screening level assessment, HED conducted a more refined assessment to reflect the actual use pattern of these inert ingredients in pesticide formulations as described above for the acute dietary assessment. The chronic dietary (food and water) exposure estimates are 27% of the cPAD for the U.S. population and 85% of the cPAD for children 1-2 yrs old, the most highly exposed population subgroup when the assessment was refined based on the proposed maximum amounts these inerts are likely to be in final formulations. See Table 5.4.4, below for a summary of results.

5.5.3 Cancer Dietary Exposure and Risk

HED has not identified any concerns for carcinogenicity relating to the AAPs; therefore, a cancer dietary exposure assessment was not performed.

5.5.4. Summary of Dietary Exposure and Risk Assessment Results

The results of the acute and chronic dietary risk assessment are shown in the summary table, below.

Table 5.5.4. Summary of Dietary (Food and Water) Exposure and Risk for AAPs

Population Subgroup	Acute Dietary (95th Percentile)		Chronic Dietary	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD
General U.S. Population	0.113767	16	0.039989	27
All Infants (< 1 year old)	0.252003	35	0.084945	57
Children 1-2 years old	**0.315197**	**44**	**0.127307**	**85**
Children 3-5 years old	0.230332	32	0.094739	63
Children 6-12 years old	0.133067	18	0.052682	35
Youth 13-19 years old	0.081379	11	0.030045	20
Adults 20-49 years old	0.079350	11	0.030455	20
Adults 50+ years old	0.079669	11	0.032072	21
Females 13-49 years old	0.081334	11	0.030647	20

The most highly exposed subgroup is bolded.

6.0 Residential (Non-Occupational) Exposure/Risk Characterization

A screening level residential exposure and risk assessment was completed for products containing alkyl amine polyalkoxylates as inert ingredients. Details of the residential exposure and risk assessment can be found in Appendix E. A summary of the residential exposure and risk assessment is presented below.

6.1 Residential Handler Exposure

Exposure Scenarios

In this assessment, the Agency selected representative scenarios, based on end-use product application methods and labeled application rates. The residential products are typically formulated as liquids in concentrates or as wettable powders. The AAPs themselves have no pesticidal properties, and are added to pesticide formulations for their adjuvant properties. According the petition submitted by the JITF CST4, the AAPs are not added to any pesticides intended for indoor use (i.e., where the Agency would

typically assess crack and crevice/pet uses)[1]. Therefore, HED assumed no indoor uses exist; but this should be validated by RD, and restrictions on use of these inerts for indoor-use products should be mandated.

For each of the use scenarios, the Agency assessed residential handler (applicator) inhalation and dermal exposure for outdoor scenarios with high exposure potential (i.e., exposure scenarios with high end unit exposure values) to serve as a screening assessment for all potential residential pesticides containing the AAP inert ingredients.

Mixer/Loader/Applicator High Exposure Outdoor Scenarios:

- Liquid products: Low Pressure Handwand;
- Liquid products: Hose End Sprayer
- Ready to Use (RTU): Trigger Pump Sprayer Applications;

Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessments for the AAPs. Each assumption and factor is detailed below. In addition to these factors, unit exposures were used to calculate risk estimates. These unit exposures were primarily taken from the Pesticide Handlers Exposure Database (PHED). Several of the assumptions and factors used for the assessment are similar to those used in the occupational assessment presented below. Some of the factors used in the residential scenarios are highlighted below.

The Agency also used assumptions based on the Residential Exposure Assessment Standard Operating Procedures (SOPs). The duration of exposure was assumed to be short- and intermediate-term for all residential scenarios assessed. The following assumptions were used in this assessment:

- The maximum application rate per pesticide group (herbicide/pesticide/fungicide) has been assessed for the short-term exposure duration.
- The average application rate per pesticide group (herbicide/pesticide/fungicide) has been assessed for the intermediate-term exposure duration.
- Residential risk assessments are based on estimates of what homeowners would typically treat. Per HED's Residential SOPs (1997 & 2001 revision), residential pesticide handlers are assumed to mix and use a volume of 5 gallons of product per day.
- For herbicide applications, residential handlers are assumed to use 1.125 lbs AAP per day.

This estimate is based on the following assumptions:

Five (5) gallons of formulated pesticide solution are assumed to be used per day by a residential handler (Revised Residential SOPs Area Treated, February, 2001). Consistent with the residential SOPs, the density of the formulated pesticide solution is assumed to be 9 lbs/gallon. For herbicides, 25% of the five

[1] The Joint Inert Task Force (JITF) Cluster Support Team Number 4 (CST4) presented this information verbally at the January 14th, 2009 JITF/OPP Update meeting.

gallons of formulated pesticide solution can be AAPs and the product concentrate is assumed to be diluted at a 1 to 10 ratio with water.

5 gallons formulated pesticide solution*(9 lbs/gallon)*(25% AAP)*(1 part product concentrate/10 parts water) = 1.125 lbs AAP in herbicide formulated pesticide solutions per day

- For insecticide/fungicide applications, residential handlers are assumed to use 0.45 lbs AAP per day.

This estimate is based on the following assumptions:

Five (5) gallons of formulated pesticide solution are assumed to be used per day by a residential handler (Revised Residential SOPs Area Treated, February, 2001). Consistent with the residential SOPs, the density of the formulated pesticide solution is assumed to be 9 lbs/gallon. For insecticides/fungicides, 10% of the five gallons of formulated pesticide solution can be AAPs and the product concentrate is assumed to be diluted at a 1 to 10 ratio with water.

5 gallons formulated pesticide solution*(9 lbs/gallon)*(10% AAP)*(1 part product concentrate/10 parts water) = 0.45 lbs AAP in insecticide or fungicide formulated pesticide solutions per day

- Residential exposure is assessed assuming clothing consisting of a short-sleeved shirt, short pants and no gloves or respiratory protection.

Risk Characterization

For all residential handler scenarios, risk estimates are not of concern (i.e., MOEs are all greater than 100) for both the route-specific (dermal or inhalation) assessment and for the total MOE (dermal and inhalation combined). A summary of the results are provided below in Table 6.1.

The Agency believes that the scenarios assessed in this document represent worse-case exposures and risks resulting from use of pesticide products containing the AAPs in residential environments.

Table 6.1. Short- and Intermediate-Term Exposure and Risks for Residential Handlers of the AAPs

Exposure Scenario (Formulation/ Application)	Application Rate[1] (lb inert/ day)	Area Treated Daily[2] (units)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (mg/ lb inert)[3]	Dermal Dose (mg/kg /day)[4]	Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Herbicide Mixer/Loader/Applicator Scenarios									
Liquids/ Low Pressure Handwand	1.125	1	38	0.003	0.03054	4.82×10^{-5}	490	310,000	490
Liquids/ Hose End Sprayer[9]	1.125		11	0.017	0.00884	0.000273	1,700	55,000	1,600
Liquids/ Trigger Sprayer/ Home Garden	1.125		54	0.0019	0.0434	3.05×10^{-5}	350	490,000	350
Insecticide and Fungicide Mixer/Loader/Applicator Scenarios									
Liquids/ Low Pressure Handwand	0.45	1	38	0.003	0.0122	1.93×10^{-5}	1,200	780,000	1,200
Liquids/ Hose End Sprayer[9]	0.45		11	0.017	0.0035	1.09×10^{-4}	4,200	140,000	4,100
Liquids/ Trigger Sprayer/ Home Garden	0.45		54	0.0019	0.017	1.22×10^{-5}	860	1,200,000	860

[1]Application rates are based on high end application rates of products containing inerts in the AAPs multiplied by 25% to convert to application rate of just inert in an herbicides product (Herbicide products contain maximum of 25% inert from the AAPs according to Inerts Task Force). For insecticide and fungicide application rates, the AAPs multiplied by 10% to convert to application rate of just inert in an insecticide/fungicide products. Application rates for Short-Term exposure risk estimates are based on maximum product application rates. Application rates for Intermediate-Term exposure risk estimates arer based on average product application rates.

[2]Area treated daily values are back-calculated from 5 gallons of product used per day (Revised Residential SOPs 2001).

[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 except for liquids hose end sprayer scenario (See footnote 9). All exposure scenarios assess exposure reflecting applicators wearing short-sleeved shirts and shorts and no respiratory protection.

[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)

[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6] Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7] ST Inhalation MOE = PoD (NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8] Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)
[9] Uses unit exposures from ORETF Homeowner Study (MRID 449722-01)

6.2. Residential Postapplication Exposure

Exposure Scenarios
Residential postapplication exposures result when bystanders, such as children come in contact with the AAPs in areas where end-use products have recently been applied (e.g., treated lawns or gardens). As noted above, the AAPs are not added to any pesticides intended for indoor use.

Postapplication High End Outdoor Exposure Scenarios

- Dermal exposure to treated lawns (adults/children)
- Hand-to-Mouth activity for toddlers on treated lawns (children)
- Object-to-Mouth activity for toddlers on treated lawns (children)
- Soil ingestion from treated soil (children)

The exposures from these routes and scenarios were considered individually and were also added together, where appropriate, to determine a total dose for children exposure to treated lawns. Residential postapplication exposure is assessed on the day of application, typically referred to as Day 0.

Inhalation exposures are not typically calculated for residential post-application scenarios for the formulation types applicable to the AAPs because inhalation exposures generally account for a negligible percentage of the overall body burden for most pesticide chemicals. This is particularly true for chemicals with a low vapor pressure such as the AAPs.

Exposure Data and Assumptions
A series of assumptions and exposure factors served as the basis for completing the residential postapplication risk assessments. The assumptions and factors used in the risk calculations are consistent with current HED policy for completing residential exposure assessments (i.e., *SOPs for Residential Exposure Assessment [1997 and 2001 revision]*).

Exposures to adults/children after contact with treated lawns have been addressed using the latest approaches for this scenario including:

- The adverse effects for the short- and intermediate-term dermal and inhalation endpoints are based on studies where the effects were observed in both sexes. For adult exposure, the mean for US males and females was used to estimate exposure (70 kg). For child exposure, the mean of median values for male and female 3 year olds was used to estimate exposure (15 kg).
- HED has developed standard transfer coefficient (TC) values for residential postapplication scenarios to ensure consistency in exposure assessments. For the

short-term assessment, TC values of 14,500 cm^2/hr (adults) and 5,200 cm^2/hr (children) were used. For intermediate-term risk assessment, TC values of 7,300 cm^2/hr and 2,600 cm^2/hr were used. These default transfer coefficients, found in the 2001 Residential SOPs were used to calculate postapplication exposures.

- Herbicides have a maximum of 25% by weight of AAPs in the end use product and insecticides and fungicides have a maximum of 10% by weight of the AAPs in the end use product.
- AAP application rates are derived above in Section 6.1
- Dermal absorption is assumed to be 5%.

Risks were calculated using the Margin of Exposure (MOE) approach, which is a ratio of the body burden to the toxicological PoD. Exposures were calculated by considering the potential sources of exposure (i.e., transferable residues on treated lawns), then calculating dermal and nondietary ingestion exposures.

Risk Characterization

A summary of the residential post application exposure and risk estimates are presented in Table 6.2, below. The risk estimates are expressed in terms of the MOE. In addition to estimating route specific MOEs, a total MOE was calculated for the AAPs because common toxicity endpoints were identified for the oral, dermal and inhalation routes of exposure.

Additionally, the Agency has combined risk estimates resulting from separate postapplication exposure scenarios when it is likely that they can occur simultaneously based on the use-pattern and the behavior associated with the exposed population. The combined non-dietary risks from dermal exposure and hand-to-mouth exposure on treated lawns do not demonstrate risks of concern for toddlers.

All assessed scenario risk estimates are not of concern (i.e., the MOEs for the assessed scenarios are greater than 100) for both the individual exposure scenario assessed and for the aggregate risk estimates.

Table 6.2. Residential Postapplication Short- and Intermediate-term Exposures and Risks for the AAPs

Exposure Scenario	Application Rate (lb inert/day)[1]	Exposed Population & Exposure Duration[2]	Daily Dose (mg/kg/day)[3]	MOE[4]
Herbicide Product Scenarios				
Dermal Exposure to Treated Lawns	1.125	Adult ST	0.013	1,100
		Adult IT	0.007	2,300
		Child ST	0.022	690
		Child IT	0.011	1,400
Hand-to-Mouth from Treated Lawn		Child ST	0.0168	900
		Child IT	0.00799	1,900
Object-to-Mouth from Treated Lawn		Child	0.00421	3,600
Soil Ingestion		Child	5.635×10^{-5}	270,000
Total Aggregated Exposures*		Child ST	0.0388	390
		Child IT	0.0190	790
Insecticide and Fungicide Product Scenarios				
Dermal Exposure to Treated Lawns	0.45	Adult ST	0.0052	2,900
		Adult IT	0.003	5,000
		Child ST	0.00875	1,700
		Child IT	0.004	3,800
Hand-to-Mouth from Treated Lawn		Child ST	0.0067	2,200
		Child IT	0.0032	4,700
Object-to-Mouth from Treated Lawn		Child	0.00168	8,900
Soil Ingestion		Child	2.254×10^{-5}	670,000
Total Aggregated Exposures[5]		Child ST	0.0155	970
		Child IT	0.007	2,100

[1] Application rates derived in Section 6.1
[2] ST and IT indicate short- or intermediate-term exposure durations
[3] Daily Dose = Daily Dose algorithms for various residential postapplication scenarios outlined in Appendix E.
[4] MOE = PoD (NOAEL of 15 mg/kg/day for short- & intermediate-term exposure durations)/ Daily dose (mg/kg/day)
[5] Aggregated exposures reflect the aggregation of dermal exposure to treated lawns and HTM exposure from treated lawns (for children). Total Aggregate Exposures = (NOAEL of 15 mg/kg/day for short-term exposure durations)/ [Daily dose dermal + Daily dose HTM (mg/kg/day)]

7.0 Aggregate Risk Assessments and Risk Characterization

As previously noted, the AAPs appear to have very limited use in consumer or personal care products. Given the high end dietary exposure and residential exposure screening level assessments used to address exposure and risk from the uses of the AAPs as inerts in pesticide products, and given their limited uses and low concentrations in consumer products, HED believes that the consumer care uses are unlikely to significantly impact aggregate risk.

7.1 Acute Aggregate Risk

For the alkyl amine polyalkoxylates, the acute aggregate risk includes dietary exposures to food and drinking water. Dietary (food and water) exposures and risk are discussed in Section 5.5.1 of this memorandum. Acute aggregate risks for the AAPs are not of concern.

7.2 Short-Term/Intermediate-Term Aggregate Risk

Short-term and intermediate-term aggregate risk assessments for the AAPs combine high end residential short- or intermediate-term exposures with average food and drinking water exposures, and compare this total to a short- or intermediate term PoD. Short- and intermediate-term aggregate risks are summarized in Table 7.2. Short- and intermediate-term aggregate risks are not of concern. While the MOE for short-term aggregate exposure for children is slightly below 100, HED does not consider this MOE to represent a risk of concern for the following reasons.

- The hazard assessment for the AAPs is conservative.
    - The PoDs used to calculate aggregate risks for AAPs were based on the most toxic surrogate chemical. The AAPs are actually a mixture of compounds, so it is likely that the PoD is a conservative assessment of toxicity.
    - HED traditionally considers a level of concern (LOC) for these risk assessments to be for an MOE of 100 based on the standard 10x inter and 10x intra species extrapolation safety factors. However, HED notes that for the AAPs, the primary toxic effect seen is related to the surfactants inherent function to disrupt cell membranes resulting in irritating properties to tissues. Given that HED does not expect to see a significant difference between species for this type of effect, an LOC lower than 100 may be appropriate for the non-dietary risk assessments.

- The dietary (food and water) portion of the aggregate risk assessment is a driver in the aggregate assessment and is considered to be highly conservative.
    - The highest tolerance level from the surrogate pesticides for every food is used.
    - 100% crop treated is assumed for all crops (every food eaten by a person each day has tolerance-level residues).

- Many of these high tolerances are based on very short pre-harvest intervals where there is little time for degradation.
- No consideration was given to potential degradation between harvest and consumption (use of tolerance level residues which are typically one to two orders of magnitude higher than actual residues found in monitoring data).
- Residue values were assigned to every commodity in DEEM™ with no consideration given to potential reduction in residues from washing or cooking.

- The residential portion of the assessment is based on high-end application rates and assumes a dermal absorption of 5% which is a conservative, health protective value.

- Finally, the aggregate assessment assumes that a child would receive a high-end dietary exposure with high-end dermal and hand-to-mouth exposures concurrently.

Table 7.2. Short- and Intermediate-Term Aggregate Risk Calculations for the AAPs

Population	Short- and Intermediate-Term					
	NOAEL mg/kg/day	LOC[1]	Max Allowable Exposure[2] mg/kg/day	Average Food & Water Exposure mg/kg/day	Residential Exposure[3] mg/kg/day	Aggregate MOE (food and residential)[4]
Adult Male ST/IT	15	100	0.15	0.039989	0.056430	156
Adult Female ST/IT	15	100	0.15	0.030647	0.056430	172
Child - ST	15	100	0.15	0.127307	0.0388	90
Child - IT	15	100	0.15	0.127307	0.0190	102

[1] The LOC (Level of Concern) is based on the standard inter- and intra-species uncertainty factors totaling 100.
[2] Maximum Allowable Exposure (mg/kg/day) = PoD/LOC
[3] Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure]. Adult residential exposure combines high end dermal and inhalation handler exposure (Table 6.1) with high end post application dermal exposure (Table 6.2). Children's residential exposure combines turf dermal exposure with HTM exposures (Table 6.2).
[4] Aggregate MOE = [PoD/ (Avg Food & Water Exposure + Residential Exposure)]

7.3 Long-Term Aggregate Risk

For the alkyl amine polyalkoxylates, the long-term aggregate risk includes dietary exposures to food and drinking water. Dietary (food and water) exposures and risk are discussed in Section 5.5.2 of this memorandum. Long-Term (chronic) aggregate risks for the AAPs are not of concern.

7.4 Cancer Risk

HED has not identified any concerns for carcinogenicity; therefore, an aggregate cancer dietary exposure assessment was not performed.

8.0 Occupational Exposure/Risk Pathway

Based on examination of product labels which might potentially contain the AAPs as inert ingredients, HED has determined that exposure to handlers can occur in a variety of occupational environments. Details of the occupational exposure assessment for the alkyl amine polyalkoxylates can be found in Appendix F.

The representative occupational scenarios selected by the Agency for assessment were evaluated based on likely maximum application rates for products which may contain the AAPs as inert ingredients for the short-term exposure assessment, and average application rates for products likely to contain the AAPs as inerts for the intermediate- and long-term exposure durations. Active ingredient application rates were corrected for the maximum amount of AAPs likely to be in the final formulations to determine exposure and risk from exposure to the AAPs grouped by fungicide/insecticide or herbicide. A summary of the occupational assessment is presented below.

HED traditionally considers a level of concern (LOC) for these risk assessments to be an MOE of 100 based on the standard 10X inter and 10X intra species extrapolation safety factors. However, HED notes that for the AAPs, the primary toxic effect seen is related to the surfactants' inherent function to disrupt cell membranes resulting in irritating properties to tissues. Given that HED does not expect to see a significant difference between species for this type of effect, an LOC lower than 100 may be appropriate for the non-dietary risk assessments.

8.1 Handler Risk

Exposure Scenarios

Exposure to pesticide handlers is likely during the occupational use of pesticides containing the AAPs as inert ingredients. Dermal and inhalation exposure was estimated using the Pesticide Handlers Exposure Database (PHED) and Outdoor Residential Exposure Task Force (ORETF) data. Appendix F contains additional description about the data sources and methodology used to assess occupational exposure. The quantitative exposure/risk assessment developed for occupational handlers to support the requested exemption for the AAPs is based on the following scenarios. HED notes that these scenarios were selected to represent the scenarios with the highest potential exposure.

Mixer/Loader/Applicators:

1) Mixer/Loader for aerial application- high acreage field crops (liquids)
2) Mixer/Loader for airblast application- tree nuts crops (both liquid and wettable powder)

3) Mixer/Loader for groundboom application- high acreage field crops and turf (liquids and wettable powder)
4) Applicators for aerial application- high acreage field crops (liquid)
5) Applicators for airblast- tree nut crops
6) Applicators for groundboom- high acreage field crops and turf
7) Mixer/Loader/Applicator- low pressure handwand (liquids and wettable powders)*
8) High pressure handwand- greenhouse (wettable powders)
9) Flagging- high acreage field crops (liquids)

* Uses ORETF unit exposure data. All others use PHED data.

Risk estimates were calculated using the Margin of Exposure (MOE) which is a ratio of the toxicological PoD to the daily dose. Daily dose values are calculated by first calculating exposures by considering application parameters (i.e., rate and area treated) along with unit exposures. Exposures are then normalized by body weight to calculate dose levels. Dermal and inhalation short-term exposure is compared to the dermal and inhalation PoD of 30 mg/kg/day. Dermal and inhalation intermediate-term exposure is compared to the intermediate term dermal and inhalation PoD of 15 mg/kg/day. For the scenarios where applicable, dermal and inhalation intermediate-term exposure is compared to the long-term dermal and inhalation PoD of 15 mg/kg/day. For both short- and intermediate-term dermal assessments, exposures were adjusted for 5% dermal absorption for comparison to the POD from an oral toxicity study, and inhalation toxicity was assumed to be equivalent to oral toxicity. A combined dermal and inhalation MOE was also calculated for each exposure duration for the AAPs since common toxicity endpoints were identified for both the dermal and inhalation routes of exposure. To assess handler risks, the Agency used surrogate unit exposure data from the Pesticide Handlers Exposure Database (PHED), and ORETF data.

Occupational handler exposure assessments are completed by the Agency using different levels of personal protection. The Agency typically evaluates all exposures with a tiered approach. The lowest tier is represented by the baseline exposure scenario followed by increasing the levels of personal protection represented by personal protective equipment or PPE (e.g., gloves, extra clothing, and respirators) and engineering controls (e.g., closed cabs and closed loading systems). This approach is always used by the Agency in order to be able to define label language using a risk-based approach and not based on generic requirements for label language. In addition, the minimal level of adequate protection for a chemical is generally considered by the Agency to be the most practical option for risk reduction. The levels of protection that form the basis for the calculations in this assessment include:

- **Baseline Exposure Scenario:** Represents typical work clothing; a long-sleeved shirt, long pants, socks, and shoes. Chemical-resistant gloves or respiratory protection are not included in this scenario.

- **Baseline Plus Gloves:** Represents the baseline exposure scenario with the use of chemical-resistant gloves. No respiratory protection is included in this scenario.

- **Engineering Controls:** Represents the use of an appropriate engineering control such as a closed cockpit. Engineering controls are not applicable to handheld application methods which have no known devices that can be used to routinely lower the exposures for these methods.

The following assumptions and factors were used in order to complete the exposure and risk assessment for occupational handlers/applicators:

- All worker scenarios were assumed to be short- and intermediate-term in exposure durations (i.e., 1-30 days and 1-6 months) with the exception of greenhouse/hothouse applications.
- For scenarios where greenhouse/hothouse applications are possible, a long-term exposure duration (6+ months) has also been calculated.
- The exposure assessment assumes an 8 hour work day.
- The maximum application rate per pesticide group (herbicide/pesticide/fungicide) has been assessed for the short-term exposure duration.
- The average application rate per pesticide group (herbicide/pesticide/fungicide) has been assessed for the intermediate-term exposure duration.
- A body weight of 70 kg was assumed because the relevant toxicological PoDs were not gender specific.
- All exposures were assessed at the baseline exposure scenario.
- For high acreage crops (e.g. corn, soybeans) where applicators can mix/load large quantities of pesticide, exposure assessments have also been completed for the baseline exposure scenario plus chemical-resistant gloves (described in the previous paragraph), and no respiratory protection.

Risk Characterization:

HED initially assessed handler exposure and risks for AAPs in fungicides, herbicides and insecticides at baseline PPE (long pants, a long-sleeved shirt, shoes, socks, no chemical-resistant gloves, and no respiratory protection) which HED considers to be the typical minimal worker clothing. When these assessments indicated that there were potential risks of concern for scenarios where workers would be handling large quantities of pesticide for high volume operations typically involving aerial applications to high acreage crops, HED repeated the assessments and included additional PPE (i.e., chemical-resistant gloves for pesticide handlers). The Agency believes workers handling large volumes of pesticides will be wearing chemical-resistant gloves.

When handlers are wearing typical worker clothing (i.e., baseline PPE) the majority of occupational handler scenarios do not indicate risks of concern. For the occupational handler scenarios which involve the handling of large volumes of pesticides, those which EPA believes that handlers will be wearing chemical-resistant gloves, occupational handler scenarios do not indicate risks of concern with the addition of chemical-resistant gloves to baseline PPE (i.e., baseline plus gloves). For the occupational scenarios that involve mixer loader applicators applying pesticides containing an AAP formulated as a wettable powder with a low pressure handwand to ornamentals in a greenhouse

environment, calculated risks resulted in MOEs below 100 when only traditional work clothes were assumed. Since the Agency does not believe that it is routine for these workers to wear gloves for these scenarios, an assessment was provided showing MOEs when the percent of AAP in the final formulation was reduced. For herbicides the assessments were provided reducing the cap from the proposed maximum of 25% to 20%, 15%, 10% and 5%. For insecticides and fungicides containing the AAPs, assessments were provided showing the impact on MOEs of reducing the maximum allowed amount in the final formulation from the proposed maximum of 10% to 8%, 6% and 5%.

Table 8.1.1. Exposure and Risks for Occupational Handlers of the AAPs in Herbicide Products (All Exposure Durations) at Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader Scenarios									
Liquids/ Aerial Application/ High Acreage Crops (ST)	2.6	1200	2.9	1.2	6.46	0.0535	**2**	280	**2**
Liquids/ Aerial Application/ High Acreage Crops (IT)	0.5				1.24	0.0103	**12**	1,500	**12**
Liquids/ Airblast/ Nut Tree (ST)	1.8	40			0.15	0.00123	100	12,000	100
Liquids/ Airblast/ Nut Tree (IT)	0.8				0.0663	0.00055	230	27,000	220
Liquids/ Groundboom/ High Acreage Crops (ST)	2.6	200			1.077	0.0089	**14**	1,700	**14**
Liquids/ Groundboom/ High Acreage Crops (IT)	0.5				0.207	0.001714	**72**	8,800	**72**
Liquids/ Groundboom/ Turf (ST)	2.6	40			0.215	0.00178	**70**	8,500	**69**
Liquids/ Groundboom/ Turf (IT)	0.5				0.0414	0.00034	360	44,000	360
Liquids/ Low Pressure Handwand/ Turf (ST)	1.8	5			0.0186	0.000154	800	95,000	800
Liquids/ Low Pressure Handwand/ Turf (IT)	1.8				0.0186	0.000154	800	97,000	800
Wettable Powder/ Airblast/ Nut Tree (ST)	0.4	40	3.7	43	0.0423	0.0098	350	1,500	290
Wettable Powder/ Airblast/ Nut Tree (IT)	0.4				0.0423	0.0098	350	1,500	290
Wettable Powder/ Groundboom/ High Acreage Crops (ST)	0.4	200			0.2114	0.05	**70**	300	**60**
Wettable Powder/ Groundboom/ High Acreage Crops (IT)	0.25				0.1321	0.031	110	490	**92**
Wettable Powder/ Groundboom/ Turf (ST)	0.4	40			0.0423	0.0098	350	1,500	290
Wettable Powder/ Groundboom/ Turf (IT)	0.25				0.026	0.00614	570	2,400	460
Wettable powder/ Low Pressure Handwand/ Turf (ST)	1.8	5			0.0238	0.0055	630	2,700	510
Wettable powder/ Low Pressure Handwand/ Turf (IT)	1.8				0.0238	0.0055	630	2,700	510
Applicator Scenarios									

Table 8.1.1. Exposure and Risks for Occupational Handlers of the AAPs in Herbicide Products (All Exposure Durations) at Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Liquid/ Aerial Application/ High Acreage Crops (ST)[9]	2.6	1200	Eng control only: 0.0055	Eng control only: 0.068	0.0123	0.003	1,200	5,000	1,000
Liquid/ Aerial Application/ High Acreage Crops (IT)[9]	0.5				0.0024	0.0006	6,400	26,000	5,100
Airblast/ Nut Tree (ST)	0.4	40	0.36	4.5	0.00411	0.00103	3,600	15,000	2,900
Airblast/ Nut Tree (IT)	0.4				0.00411	0.00103	3,600	15,000	2,900
Groundboom/ High Acreage Crops (ST)	2.6	200	0.014	0.74	0.0052	0.0055	2,900	2,700	1,400
Groundboom/ High Acreage Crops (IT)	0.5				0.001	0.0011	15,000	14,000	7,300
Groundboom/ Turf (ST)	2.6	40			0.00104	0.0011	14,000	14,000	7,000
Groundboom/ Turf (IT)	0.5				0.0002	0.0002	75,000	71,000	36,000
Mixer/Loader/Applicator Scenarios									
Low Pressure Handwand/ Turf (ORETF data) (ST)[10]	1.8	5	no data	6.6	NA	0.00085	NA	18,000	NA
Low Pressure Handwand/ Turf (ORETF data) (IT)[10]	1.8				NA	0.00085	NA	18,000	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (ST)[10]	1.8	5	no data	1100	NA	0.1414	NA	110	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (IT)[10]	1.8				NA	0.1414	NA	110	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (LT)[10]	1.8				NA	0.1414	NA	110	NA
Liquid/ Low Pressure Handwand/ Ornamentals (ST)	1.8	5	100	30	0.6429	0.0039	**23**	3,900	**23**
Liquid/ Low Pressure Handwand/ Ornamentals (IT)	1.8				0.6429	0.0039	**23**	3,900	**23**
Liquid/ Low Pressure Handwand/ Ornamentals (LT)	1.8				0.6429	0.0039	**23**	3,900	**23**
Flagger Scenarios									
Liquid/ Flagger/ High Acreage Crops (ST)	2.6	1200	0.011	0.35	0.0245	0.0156	600	960	380
Liquid/ Flagger/ High Acreage Crops (IT)	0.5				0.0047	0.003	3,200	5,000	1,900

[1]Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by 25% to convert to application rate of just inert in an herbicides product (Herbicide products contain a maximum of 25% inert AAPs according to Inerts Task Force). Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate-term (IT) and long-term (LT) exposures are based on average application rates. Baseline Exposure Scenario represents typical work clothing, no gloves.

[2]Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario of concern.

[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline exposure scenario and baseline inhalation exposure except for aerial applicator scenarios, which assess inhalation and dermal exposures with engineering controls.

[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)

[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)

[6]Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)

[7]ST Inhalation MOE = PoD (NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)

[8]Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)

[9]Aerial applicators do not have baseline exposure: only engineering control exposure can be assessed. All other exposure scenarios assess the baseline exposure scenario and baseline inhalation exposure.
[10]These scenarios have baseline inhalation unit exposures, but not baseline dermal unit exposures. The M/L/A scenario assessed in Table 8.1.1. results in a higher exposure (and therefore is health protective) than either of the two "NA" scenarios shown at baseline plus gloves dermal exposure.

Table 8.1.2. Exposure and Risks for Occupational Handlers of AAPs in Herbicide Products (All Exposure Durations) with Baseline Plus Gloves for High Acreage Mixer/ Loader Scenarios and Turf

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline + Gloves Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline + Gloves Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader Scenarios									
Liquids/ Aerial Application/ High Acreage Crops (ST)	2.6	1200	0.023	1.2	0.0513	0.0535	290	280	150
Liquids/ Aerial Application/ High Acreage Crops (IT)	0.5				0.0099	0.0103	1,500	1,500	750
Liquids/ Groundboom/ High Acreage Crops (ST)	2.6	200			0.00854	0.0089	1,800	1,700	850
Liquids/ Groundboom/ High Acreage Crops (IT)	0.5				0.00164	0.001714	9,100	8,800	4,500
Liquids/ Groundboom/ Turf (ST)	2.6	40			0.0017	0.0018	8,800	8,400	4,300
Liquids/ Groundboom/ Turf (IT)	0.5				0.00033	0.00034	47,000	44,000	22,000
Wettable Powder/ Groundboom/ High Acreage Crops (ST)	0.4	200	0.17	43	0.00971	0.05	1,500	300	250
Wettable Powder/ Groundboom/ High Acreage Crops (IT)	0.25				0.00610	0.031	2,500	490	410

[1]Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by 25% to convert to application rate of just inert in an herbicides product (Herbicide products contain maximum of 25% inert from the AAPs according to Inerts Task Force). Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate-term (IT) and long-term (LT) exposures are based on average application rates.
[2]Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario of concern.
[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline plus gloves plus baseline inhalation exposure except for aerial applicator scenarios, which assess inhalation and dermal exposures with engineering controls.
[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)
[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6]Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7]ST Inhalation MOE = PoD (NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8]Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)
*Aerial applicators do not have baseline exposure: only engineering control exposure can be assessed. All other exposure scenarios assess baseline plus gloves and baseline inhalation exposure.

Table 8.1.3: Exposure and Risks for Occupational Handlers of AAPs in Herbicide Products Used in Low Pressure Handwand Applications to Ornamentals in Greenhouses (All Exposure Durations) at Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader/Applicator for Herbicide Products with 20% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	1.44	5	100	30	0.514	0.0031	**29**	4,900	**29**
Mixer/Loader/Applicator for Herbicide Products with 15% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	1.08	5	100	30	0.386	0.0023	**39**	6,500	**39**
Mixer/Loader/Applicator for Herbicide Products with 10% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	0.72	5	100	30	0.257	0.0015	**58**	9,700	**58**
Mixer/Loader/Applicator for Herbicide Products with 5% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	0.36	5	100	30	0.129	0.00077	120	19,000	120

[1]Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by variable % AAP in formulation to convert to application rate of just inert in an herbicide product. Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate-term (IT) and long-term (LT) exposures are based on average application rates.
[2]Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario of concern.
[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline exposure scenario plus baseline inhalation exposure
[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)
[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6] Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7] Inhalation MOE = PoD (NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8]Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)

Table 8.1.4. Exposure and Risks for Occupational Handlers of AAPs in Insecticide Products (All Exposure Durations) at Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader Scenarios									
Liquids/ Aerial Application/ High Acreage Crops (ST)	0.2	1200	2.9	1.2	0.497	0.00411	**30**	3,600	**30**
Liquids/ Aerial Application/ High Acreage Crops (IT)	0.07				0.174	0.00144	**86**	10,400	**86**

Table 8.1.4. Exposure and Risks for Occupational Handlers of AAPs in Insecticide Products (All Exposure Durations) at Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Liquids/ Airblast/ Nut Tree (ST)	0.9	40			0.075	0.00062	200	24,000	200
Liquids/ Airblast/ Nut Tree (IT)	0.25				0.0207	0.00017	720	88,000	720
Liquids/ Groundboom/ High Acreage Crops (ST)	0.2	200			0.0829	0.00069	180	22,000	180
Liquids/ Groundboom/ High Acreage Crops (IT)	0.07				0.029	0.00024	520	63,000	520
Liquids/ Groundboom/ Turf (ST)	0.2	40			0.0166	0.000137	900	110,000	900
Liquids/ Groundboom/ Turf (IT)	0.07				0.0058	0.000048	2,600	310,000	2,600
Liquids/ Low Pressure Handwand/ Turf (ST)	0.72	5			0.0075	0.00006	2,000	240,000	2,000
Liquids/ Low Pressure Handwand/ Turf (IT)	0.72				0.0075	0.00006	2,000	240,000	2,000
Wettable Powder/ Airblast/ Nut Tree (ST)	0.6	40	3.7	43	0.0634	0.01474	240	1,000	190
Wettable Powder/ Airblast/ Nut Tree (IT)	0.3				0.0317	0.00737	470	2,000	380
Wettable Powder/ Groundboom/ High Acreage Crops (ST)	0.2	200			0.1057	0.025	140	600	120
Wettable Powder/ Groundboom/ High Acreage Crops (IT)	0.07				0.037	0.0086	410	1,700	330
Wettable Powder/ Groundboom/ Turf (ST)	0.2	40			0.02	0.0049	700	3,100	600
Wettable Powder/ Groundboom/ Turf (IT)	0.07				0.0074	0.00172	2,000	8,700	1,600
Wettable powder/ Low Pressure Handwand/ Turf (ST)	0.72	5			0.0095	0.0022	1,600	7,000	1,300
Wettable powder/ Low Pressure Handwand/ Turf (IT)	0.72				0.0095	0.0022	1,600	6,800	1,300
Applicator Scenarios									
Liquid/ Aerial Application/ High Acreage Crops (ST)[9]	0.2	1200	Eng control only: 0.0055	Eng control only: 0.068	0.0009	0.0002	16,000	65,000	13,000
Liquid/ Aerial Application/ High Acreage Crops (IT)[9]	0.07				0.0003	0.0001	45,000	180,000	36,000
Airblast/ Nut Tree (ST)	0.9	40	0.36	4.5	0.0093	0.002314	1,600	6,500	1,300

Table 8.1.4. Exposure and Risks for Occupational Handlers of AAPs in Insecticide Products (All Exposure Durations) at Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Airblast/ Nut Tree (IT)	0.25				0.0026	0.000643	5,800	23,000	4,700
Groundboom/ High Acreage Crops (ST)	0.2	200	0.014	0.74	0.0004	0.000423	38,000	35,000	18,000
Groundboom/ High Acreage Crops (IT)	0.07				0.00014	0.000148	110,000	100,000	52,000
Groundboom/ Turf (ST)	0.2	40			0.00008	0.000085	190,000	180,000	90,000
Groundboom/ Turf (IT)	0.07				0.00003	0.00003	540,000	510,000	260,000
Mixer/Loader/ Applicator Scenarios									
Low Pressure Handwand/ Turf (ORETF data) (ST)[10]	0.72	5	no data	6.6	NA	0.00034	NA	44,000	NA
Low Pressure Handwand/ Turf (ORETF data) (IT)[10]	0.72				NA	0.00034	NA	44,000	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (ST)[10]	0.72		no data	1100	NA	0.05657	NA	270	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (IT)[10]	0.72				NA	0.05657	NA	270	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (LT)[10]	0.72				NA	0.05657	NA	270	NA
Liquid/ Low Pressure Handwand/ Ornamentals (ST)	0.72	5	100	30	0.257	0.00154	**58**	19,000	**58**
Liquid/ Low Pressure Handwand/ Ornamentals (IT)	0.72				0.257	0.00154	**58**	9,700	**58**
Liquid/ Low Pressure Handwand/ Ornamentals (LT)	0.72				0.257	0.00154	**58**	9,700	**58**
Flagger Scenarios									
Liquid/ Flagger/ High Acreage Crops (ST)	0.2	1200	0.011	0.35	0.0019	0.0012	7,900	13,000	4,800
Liquid/ Flagger/ High Acreage Crops (IT)	0.07				0.00066	0.00042	23,000	36,000	14,000

[1]Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by 10% to convert to application rate of just inert in an insecticide product (Insecticide products contain maximum of 10% inert from the AAPs according to Inerts Task Force). Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate- (IT) and long-term (LT) exposures are based on average application rates.
[2]Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario.
[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline exposure scenario and baseline inhalation exposure except for aerial applicator scenarios, which assess inhalation and dermal exposures with engineering controls.
[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)
[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6] Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7]ST Inhalation MOE = PoD (NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8]Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)
[9]Aerial applicators do not have baseline exposure: only engineering control exposure can be assessed. All other exposure scenarios assess the baseline exposure scenario and baseline inhalation exposure.
[10]These scenarios have baseline inhalation unit exposures, but not baseline dermal unit exposures. The M/L/A scenario assessed in Table 8.1.4. results in a higher exposure (and therefore is health protective) than either of the two "NA" scenarios shown at baseline plus gloves dermal exposure.

Table 8.1.5. Exposure and Risks for Occupational Handlers of AAPs in Insecticide Products (All Exposure Durations) with Baseline Plus Gloves for High Acreage Mixer/ Loader Scenarios

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline + Gloves Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline + Gloves Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader Scenarios									
Liquids/ Aerial Application/ High Acreage Crops (ST)	0.2	1200	0.023	1.2	0.00394	0.00411	3,800	3,600	1,900
Liquids/ Aerial Application/ High Acreage Crops (IT)	0.07				0.00138	0.00144	11,000	10,400	5,300

[1]Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by 10% to convert to application rate of just inert in an insecticide product (Insecticide products contain maximum of 10% inert from the AAPs according to Inerts Task Force). Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate-term (IT) and long-term (LT) exposures are based on average application rates.
[2]Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario of concern.
[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline plus gloves and baseline inhalation exposure except for aerial applicator scenarios, which assess inhalation and dermal exposures with engineering controls.
[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)
[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6] Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7]ST Inhalation MOE = PoD (NOAEL of 30 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8]Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)
*Aerial applicators do not have baseline exposure: only engineering control exposure can be assessed. All other exposure scenarios assess baseline plus gloves and baseline inhalation exposure.

Table 8.1.6: Exposure and Risks for Occupational Handlers of AAPs in Insecticides Products Used in Low Pressure Handwand Applications to Ornamentals in Greenhouses (All Exposure Durations) at Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader/Applicator for Insecticides Products with 8% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	0.576	5	100	30	0.2057	0.0012	**73**	12,000	**72**
Mixer/Loader/Applicator for Insecticides Products with 6% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	0.432	5	100	30	0.1543	0.0009	**97**	16,000	**97**
Mixer/Loader/Applicator for Insecticides Products with 5% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	0.36	5	100	30	0.129	0.00077	120	19,000	120

[1]Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by variable % AAP in formulation to convert to application rate of just inert in an insecticide product. Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate-term (IT) and long-term (LT) exposures are based on average application rates.
[2]Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario of concern.
[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline exposure scenario and baseline inhalation exposure
[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)
[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6] Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7]ST Inhalation MOE = PoD (NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8]Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)

Table 8.1.7. Exposure and Risks for Occupational Handlers of AAPs in Fungicide Products (All Exposure Durations) with Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader Scenarios									
Liquids/ Aerial Application/ High Acreage Crops (ST)	0.5	1200	2.9	1.2	1.243	0.010286	**12**	1,500	**12**
Liquids/ Aerial Application/ High Acreage Crops (IT)	0.07				0.174	0.00144	**86**	10,000	**86**
Liquids/ Airblast/ Nut Tree (ST)	1.1	40			0.09114	0.000754	160	20,000	160

Table 8.1.7. Exposure and Risks for Occupational Handlers of AAPs in Fungicide Products (All Exposure Durations) with Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Liquids/ Airblast/ Nut Tree (IT)	0.3				0.0249	0.000206	600	73,000	600
Liquids/ Groundboom/ High Acreage Crops (ST)	0.5	200			0.207	0.001714	**70**	9,000	**70**
Liquids/ Groundboom/ High Acreage Crops (IT)	0.07				0.029	0.00024	520	63,000	510
Liquids/ Groundboom/ Turf (ST)	0.5	40			0.0414	0.000343	360	44,000	360
Liquids/ Groundboom/ Turf (IT)	0.07				0.0058	0.000048	2,600	310,000	2,600
Liquids/ Low Pressure Handwand/ Turf (ST)	0.72	5			0.0075	0.000062	2,000	240,000	2,000
Liquids/ Low Pressure Handwand/ Turf (IT)	0.72				0.0075	0.000062	2,000	240,000	2,000
Wettable Powder/ Airblast/ Nut Tree (ST)	0.7	40	3.7	43	0.074	0.0172	200	870	170
Wettable Powder/ Airblast/ Nut Tree (IT)	0.2				0.02114	0.004914	710	3,100	580
Wettable Powder/ Groundboom/ High Acreage Crops (ST)	0.1	200			0.0529	0.012286	280	1,200	230
Wettable Powder/ Groundboom/ High Acreage Crops (IT)	0.06				0.03171	0.00737	470	2,000	380
Wettable Powder/ Groundboom/ Turf (ST)	0.1	40			0.0106	0.002457	1,400	6,000	1,200
Wettable Powder/ Groundboom/ Turf (IT)	0.06				0.0063	0.00147	2,400	10,000	1,900
Wettable powder/ Low Pressure Handwand/ Turf (ST)	0.72	5			0.00951	0.002211	1,600	6,800	1,300
Wettable powder/ Low Pressure Handwand/ Turf (IT)	0.72				0.00951	0.002211	1,600	6,800	1,300
Applicator Scenarios									
Liquid/ Aerial Application/ High Acreage Crops (ST)[9]	0.5	1200	Eng control only: 0.0055	Eng control only: 0.068	0.0024	0.0006	6,500	25,000	5,000
Liquid/ Aerial Application/ High Acreage Crops (IT)[9]	0.07				0.0003	0.0001	45,000	180,000	36,000
Airblast/ Nut Tree (ST)	0.7	40	0.36	4.5	0.0072	0.0018	2,100	8,500	1,700
Airblast/ Nut Tree (IT)	0.3				0.0031	0.000771	4,900	19,000	3,900

Table 8.1.7. Exposure and Risks for Occupational Handlers of AAPs in Fungicide Products (All Exposure Durations) with Baseline Exposure Scenario

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Groundboom/ High Acreage Crops (ST)	0.5	200	0.014	0.74	0.001	0.001057	15,000	14,000	7,500
Groundboom/ High Acreage Crops (IT)	0.07				0.00014	0.000148	110,000	100,000	52,000
Groundboom/ Turf (ST)	0.5	40			0.0002	0.000211	75,000	70,000	37,000
Groundboom/ Turf (IT)	0.07				0.00003	0.000029	540,000	510,000	260,000
Mixer/Loader/ Applicator Scenarios									
Low Pressure Handwand/ Turf (ORETF data) (ST)[10]	0.72	5	NA	6.6	NA	0.000339	NA	44,000	NA
Low Pressure Handwand/ Turf (ORETF data) (IT)[10]	0.72				NA	0.000339	NA	44,000	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (ST)[10]	0.72		NA	1100	NA	0.05657	NA	270	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (IT)[10]	0.72				NA	0.05657	NA	270	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals (LT)[10]	0.72				NA	0.05657	NA	270	NA
Liquid/ Low Pressure Handwand/ Ornamentals (ST)	0.72	5	100	30	0.257	0.001543	**58**	9,700	**58**
Liquid/ Low Pressure Handwand/ Ornamentals (IT)	0.72				0.257	0.001543	**58**	9,700	**58**
Liquid/ Low Pressure Handwand/ Ornamentals (LT)	0.72				0.257	0.001543	**58**	9,700	**58**
Flagger Scenarios									
Liquid/ Flagger/ High Acreage Crops (ST)	0.5	1200	0.011	0.35	0.0047	0.003	3,200	5,000	1,900
Liquid/ Flagger/ High Acreage Crops (IT)	0.07				0.00066	0.00042	23,000	36,000	14,000

[1]Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by 10% to convert to application rate of just inert in an fungicide product (Fungicide products contain maximum of 10% inert from the AAPs according to the Inerts Task Force). Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate-term (IT) exposures are based on average application rates.

[2]Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario of concern.

[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline exposure scenario and baseline inhalation exposure except for aerial applicator scenarios, which assess inhalation and dermal exposures with engineering controls.

[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)

[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6] Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7] ST Inhalation MOE = PoD (a NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8] Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)
[9] Aerial applicators do not have baseline exposure: only engineering control exposure can be assessed. All other exposure scenarios assess the baseline exposure scenario and baseline inhalation exposure.
[10] These scenarios have baseline inhalation unit exposures, but not baseline dermal unit exposures. The M/L/A scenario assessed in Table 8.1.7. results in a higher exposure (and therefore is health protective) than either of the two "NA" scenarios shown at baseline plus gloves dermal exposure.

Table 8.1.8. Exposure and Risks for Occupational Handlers of AAPs in Fungicide Products (All Exposure Durations) with Baseline Plus Gloves for High Acreage Mixer/ Loader Scenarios

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline + Gloves Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline + Gloves Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader Scenarios									
Liquids/ Aerial Application/ High Acreage Crops (ST)	0.5	1200	0.023	1.2	0.00986	0.010286	1,500	1,500	750
Liquids/ Aerial Application/ High Acreage Crops (IT)	0.07				0.00138	0.00144	11,000	10,000	5,300
Liquids/ Groundboom/ High Acreage Crops (ST)	0.5	200			0.00164	0.0017	9,100	8,800	4,500
Liquids/ Groundboom/ High Acreage Crops (IT)	0.07				0.00023	0.00024	65,000	63,000	32,000

[1] Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by 10% to convert to application rate of just inert in an fungicide product (Fungicide products contain maximum of 10% inert from the AAPs according to the Inerts Task Force). Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate-term (IT) exposures are based on average application rates.
[2] Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario of concern.
[3] Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline plus gloves and baseline inhalation exposure except for aerial applicator scenarios, which assess inhalation and dermal exposures with engineering controls.
[4] Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)
[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6] Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7] ST Inhalation MOE = PoD (a NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8] Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)

Table 8.1.9: Exposure and Risks for Occupational Handlers of AAPs in Fungicides Products Used in Low Pressure Handwand Applications to Ornamentals in Greenhouses (All Exposure Durations) at Baseline Exposure Scenario (14% AAP in Formulation)

Exposure Scenario (Formulation/ Application/ Crop)	Application Rate[1] (lb inert/ A)	Area Treated Daily[2] (acres)	Dermal Unit Exposure (mg/lb inert)[3]	Inhalation Unit Exposure (ug/ lb inert)[3]	Baseline Dermal Dose (mg/kg /day)[4]	Baseline Inhalation Dose (mg/kg/ day)[5]	Baseline Dermal MOE[6]	Baseline Inhalation MOE[7]	Total MOE[8]
Mixer/Loader/Applicator for Fungicide Products with 8% AAP in Formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	0.576	5	100	30	0.2057	0.0012	**73**	12,000	**72**
Mixer/Loader/Applicator for Fungicide Products with 6% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	0.432	5	100	30	0.1543	0.0009	**97**	16,000	**97**
Mixer/Loader/Applicator for Fungicide Products with 5% AAP in formulation									
Liquids/ Low Pressure Handwand/ Ornamentals	0.36	5	100	30	0.129	0.00077	120	19,000	120

[1]Application rates are based on maximum application rates of products containing inerts in the AAPs multiplied by variable % AAP in formulation to convert to application rate of just inert in a fungicides product. Application rates for Short-term (ST) exposure risk estimates are based on maximum application rates. Application rates for Intermediate-term (IT) and long-term (LT) exposures are based on average application rates.
[2]Area treated daily values are from the EPA HED estimates of acreage treated in a single day for each exposure scenario of concern.
[3]Unit Exposure values are reported in PHED Surrogate Exposure Guide dated August 1998 or from ORETF data. All exposure scenarios assess baseline exposure scenario and baseline inhalation exposure
[4]Daily Dermal Dose = (Dermal Unit Exposure (mg inert /lb inert) * Application Rate (lb inert /A) * Area Treated (A /day))/ Body Weight (70 kg) * Dermal Absorption Factor of 5% (0.05)
[5] Daily Inhalation Dose = (Inhalation Unit Exposure (µg inert / lb inert) * Conversion Factor (1 mg /1000 µg) * Application Rate (lb inert /A) * Area Treated (A /day)) / Body Weight (70 kg)
[6] Dermal MOE = PoD (NOAEL of 15 mg/kg/day)/ Daily dermal dose (mg/kg/day)
[7]ST Inhalation MOE = PoD (NOAEL of 15 mg/kg/day) / Daily inhalation dose (mg/kg/day)
[8]Total MOE = 1/ (1/Dermal MOE + 1/Inhalation MOE)

8.2 Occupational Postapplication Risk

HED uses the term postapplication to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Postapplication exposure levels vary over time and depend on such things as the type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for postapplication exposure.

Inhalation exposures are not typically calculated for occupational post-application scenarios because inhalation exposures generally account for a negligible percentage of the overall body burden for most pesticide chemicals. This is particularly true for chemicals with a low vapor pressure such as the AAPs.

Exposure Scenarios

This assessment is considered to be a screening level estimate, demonstrating that there are minimal potential risks to workers re-entering fields treated with pesticides containing the AAPs as inert ingredients. While the AAPs are present in formulations designated for crops besides those assessed in this document, risk estimates for those occupational postapplication scenarios are expected to be less than those scenarios assessed in this document (i.e., calculated MOEs will be higher). The three occupational postapplication scenarios assessed are for postapplication activities associated with:

- Tall field/row crops (including scouting, weeding, hand harvesting sweet corn)
- Turf (golf course/sod farm) (including mowing, transplanting, hand weeding)
- Vine/Trellis crops (including scouting, training, tying, thinning, and grape girding and cane turning)

Exposure Data and Assumptions

The assumptions used in the postapplication risk assessment calculations are detailed as follows:

- The average occupational workday is assumed to be 8 hours.
- The adverse effects for the short- and intermediate-term dermal PoD's are based on studies where the effects were observed in both sexes; therefore, the body weight of 70 kg was used to estimate exposure.
- HED has developed standard transfer coefficient values for occupational postapplication scenarios to ensure consistency in exposure assessments. These standard values were used to calculate postapplication exposures.
- Anticipated post-application activities and their respective dermal transfer coefficients (TCs) are summarized in Table 8.2.1. The TC information is based on the Science Advisory Council for Exposure Policy Number 3.1.
- The transfer coefficient for sod transplanting, and hand weeding used to represent dermal exposure is from Agriculture Reentry Task Force (ARTF) data; study ARF-035 (MRID 45432303).
- Calculations of postapplication exposures are completed using maximum application rates of the products of that type of pesticide (herbicide, insecticide, or fungicide) for short-term exposures and average application rates of products for intermediate-term exposures.
- Herbicides assessed can contain a maximum of 25% AAP in any product formulation; insecticides and fungicides contain a maximum of 10% in any product formulation.
- No postapplication data were submitted for the AAPs; a default 20% of the application rate (for agricultural crops) and 5% (for turf) is considered available as a transferrable residue with a 10% default daily dissipation rate.
- Dermal absorption is assumed to be 5%.

Risks were calculated using the Margin of Exposure (MOE) approach, which is a ratio of the exposure to the toxicological PoD.

Risk Characterization

A variety of pesticide formulations contain AAPs. PPE is usually not required for worker re-entry, and therefore these postapplication risk estimates are based on the baseline exposure scenario (i.e., typical work clothing but no gloves). Typically, HED characterizes the risk estimate in relation to the restricted entry interval (REI) for a particular active ingredient. While REIs for specific products are not discussed in this risk assessment, occupational post-application scenarios assessed generally result in MOEs that do not indicate risks of concern on Day 0 (the day of application) except for two postapplication scenarios.

Occupational postapplication risk estimates are presented in Table 8.2.1. The risk estimates for the three exposure scenarios assessed resulted in MOEs do not demonstrate risks of concern (i.e., MOEs > 100) on Day 0, except for two scenarios:

1) the short-term worker postapplication activities involving herbicides on corn, specifically the hand-harvesting harvesting/ detassling scenario. That scenario resulted in an MOE of **53** on the day of application (Day 0). Assuming an herbicide application at the maximum application rate, the MOE would exceed 100 for this scenario at day 13 after application. The Agency notes that it is not expected to be typical agricultural practice to apply herbicides on the same day workers would be conducting hand harvesting and detassling activities. As noted earlier in this assessment, herbicides and insecticides are typically applied relatively early in a growing season. All other postapplication scenarios result in MOEs that do not demonstrate risks of concern on the day of application (Day 0).
2) the short-term worker postapplication activities involving insecticides on corn, specifically the hand-harvesting harvesting/ detassling scenario. That scenario resulted in an MOE of **69** on the day of application (Day 0). Assuming an insecticide application at the maximum application rate, the MOE would exceed 100 for this scenario at day 4 after application. The Agency notes that it is not expected to be typical agricultural practice to apply insecticides on the same day workers would be conducting hand harvesting and detassling activities. As noted earlier in this assessment, herbicides and insecticides are typically applied relatively early in a growing season. All other postapplication scenarios result in MOEs that do not demonstrate risks of concern on the day of application (Day 0).

Table 8.2.1. Short- and Intermediate-Term Occupational Postapplication Dermal Exposures and Risks for the AAPs

Crop & Exposure Duration	Application Rate (lb inert /A)	Work Activity	Transfer Coefficient[1] (cm^2/hr)	Day after Treatment[2]	DFR_t ($\mu g/cm^2$)[3]	Daily Dose (mg/kg/day)[4]	MOE[5]
Herbicide Product Scenarios							
Corn (ST)	2.6	Scout, weed low foliage	100	0	5.834	0.0033	4,500
		Scout, weed high foliage	400	0		0.0133	1,100
		Scout, irrigate, weed high foliage	1,000	0		0.0333	450

Table 8.2.1. Short- and Intermediate-Term Occupational Postapplication Dermal Exposures and Risks for the AAPs							
Crop & Exposure Duration	**Application Rate (lb inert /A)**	**Work Activity**	**Transfer Coefficient[1] (cm^2/hr)**	**Day after Treatment[2]**	**DFR_t ($\mu g/cm^2$)[3]**	**Daily Dose (mg/kg/day)[4]**	**MOE[5]**
		Harvesting/ detassling	17,000	0		0.5667	**26**
Days till MOE > 100							**13**
Corn (IT)	0.3	Scout, weed low foliage	100	0	0.673	0.0004	39,000
		Scout, weed high foliage	400	0		0.0015	9,700
		Scout, irrigate, weed high foliage	1,000	0		0.0038	3,900
		Harvesting/ detassling	17,000	0		0.0654	230
Grapes (Table) (ST)	1.2	Hedge, irrigate, weed, scout, train, tie	500	0	2.693	0.0077	1,900
		Scout, train, tie	1,000	0		0.0154	970
		Harvest, pull, thin, prune, train, tie	5,000	0		0.0769	200
		Cane turning, girdle	10,000	0		0.1539	100
Grapes (Table) (IT)	0.7	Hedge, irrigate, weed, scout, train, tie	500	0	1.571	0.0045	3,300
		Scout, train, tie	1,000	0		0.0090	1,700
		Harvest, pull, thin, prune, train, tie	5,000	0		0.0449	330
		Cane turning, girdle	10,000	0		0.0898	170
Turf/ sod (ST)	2.6	Mowing	500	0	1.458	0.004	3,800
		Transplant, weed, harvest	6,800	0		0.057	260
Turf/ Sod (IT)	0.3	Mowing	500	0	0.168	0	31,000
		Transplant, weed, harvest*	6,800	0		0.007	2,300
Insecticide Product Scenarios							
Corn (ST)	1.0	Scout, weed low foliage	100	0	2.244	0.0013	12,000
		Scout, weed high foliage	400	0		0.0051	2,900
		Scout, irrigate, weed high foliage	1,000	0		0.0128	1,200
		Harvesting/ detassling	17,000	0		0.2180	**69**
Days till MOE > 100							**4**

Table 8.2.1. Short- and Intermediate-Term Occupational Postapplication Dermal Exposures and Risks for the AAPs

Crop & Exposure Duration	Application Rate (lb inert /A)	Work Activity	Transfer Coefficient[1] (cm^2/hr)	Day after Treatment[2]	DFR_t ($\mu g/cm^2$)[3]	Daily Dose (mg/kg/day)[4]	MOE[5]
Corn (IT)	0.1	Scout, weed low foliage	100	0	0.224	0.0001	120,000
		Scout, weed high foliage	400	0		0.0005	29,000
		Scout, irrigate, weed high foliage	1,000	0		0.0013	12,000
		Harvesting/ detassling	17,000	0		0.0218	690
Grapes (Table) (ST)	0.7	Hedge, irrigate, weed, scout, train, tie	500	0	1.571	0.0045	3,300
		Scout, train, tie	1,000	0		0.009	1,700
		Harvest, pull, thin, prune, train, tie	5,000	0		0.0449	330
		Cane turning, girdle	10,000	0		0.0898	170
Grapes (Table) (IT)	0.3	Hedge, irrigate, weed, scout, train, tie	500	0	0.673	0.0019	7,800
		Scout, train, tie	1,000	0		0.0038	3,900
		Harvest, pull, thin, prune, train, tie	5,000	0		0.0192	780
		Cane turning, girdle	10,000	0		0.0385	390
Turf/ sod (ST)	1.0	Mowing	500	0	0.561	0.002	10,000
		Transplant, weed, harvest	6,800	0		0.022	700
Turf/ Sod (IT)	0.1	Mowing	500	0	0.056	0	94,000
		Transplant, weed, harvest*	6,800	0		0.002	6,900
Fungicide Product Scenarios							
Corn (ST)	0.5	Scout, weed low foliage	100	0	1.122	0.0006	24,000
		Scout, weed high foliage	400	0		0.0026	6,000
		Scout, irrigate, weed high foliage	1,000	0		0.0064	2,400
		Harvesting/ detassling	17,000	0		0.1090	140
Corn (IT)	0.1	Scout, weed low foliage	100	0	0.224	0.0001	120,000
		Scout, weed high foliage	400	0		0.0005	29,000

Table 8.2.1. Short- and Intermediate-Term Occupational Postapplication Dermal Exposures and Risks for the AAPs							
Crop & Exposure Duration	**Application Rate (lb inert /A)**	**Work Activity**	**Transfer Coefficient[1] (cm^2/hr)**	**Day after Treatment[2]**	**DFR_t (µg/cm^2)[3]**	**Daily Dose (mg/kg/day)[4]**	**MOE[5]**
Grapes (Table) (ST)	0.5	Scout, irrigate, weed high foliage	1,000	0	1.122	0.0013	12,000
		Harvesting/ detassling	17,000	0		0.0218	690
		Hedge, irrigate, weed, scout, train, tie	500	0		0.0032	4,700
		Scout, train, tie	1,000	0		0.0064	2,400
		Harvest, pull, thin, prune, train, tie	5,000	0		0.0321	470
		Cane turning, girdle	10,000	0		0.0641	240
Grapes (Table) (IT)	0.2	Hedge, irrigate, weed, scout, train, tie	500	0	0.449	0.0013	12,000
		Scout, train, tie	1,000	0		0.0064	2,300
		Harvest, pull, thin, prune, train, tie	5,000	0		0.0128	1,200
		Cane turning, girdle	10,000	0		0.0256	580
Turf/ sod (ST)	0.5	Mowing	500	0	0.28	0.001	19,000
		Transplant, weed, harvest*	6,800	0		0.011	1,400
Turf/ Sod (IT)	0.1	Mowing	500	0	0.056	0	94,000
		Transplant, weed, harvest*	6,800	0		0.002	6,900

* The TC from this exposure scenario uses ARTF data - study ARF-035 (MRID 45432303).

9.0 Environmental Justice

Potential areas of environmental justice concerns, to the extent possible, were considered in this human health risk assessment, in accordance with U.S. Executive Order 12898, "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations," http://www.eh.doe.gov/oepa/guidance/justice/eo12898.pdf).

As a part of every pesticide risk assessment, OPP considers a large variety of consumer subgroups according to well-established procedures. In line with OPP policy, HED estimates risks to population subgroups from pesticide exposures that are based on patterns of that subgroup's food and water consumption, and activities in and around the home that involve pesticide use in a residential setting. Extensive data on food consumption patterns are compiled by the USDA under the Continuing Survey of Food Intake by Individuals (CSFII) and are used in pesticide risk assessments for all registered

food uses of a pesticide. These data are analyzed and categorized by subgroups based on age, season of the year, ethnic group, and region of the country. Additionally, OPP is able to assess dietary exposure to smaller, specialized subgroups and exposure assessments are performed when conditions or circumstances warrant. Whenever appropriate, non-dietary exposures based on home use of pesticide products and associated risks for adult applicators and for toddlers, youths, and adults entering or playing on treated areas postapplication are evaluated. Further considerations are currently in development as OPP has committed resources and expertise to the development of specialized software and models that consider exposure to bystanders and farm workers as well as lifestyle and traditional dietary patterns among specific subgroups.

10.0 Human Studies

This assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide. These studies, listed below, have received the appropriate ethical review for use in risk assessment.

> The PHED Task Force, 1998. The Pesticide Handler Exposure Database (PHED), Version 1.1. Task Force members: Health Canada, U.S. Environmental Protection Agency, the California Department of Pesticide regulation, and the American Crop Protection Association; released August 1998.
>
> ORETF Handler Studies (MRID 44972201): Outdoor Residential Exposure Task

APPENDIX A

A.1 Acute Toxicity Profile for Alkyl Amine Polyalkoxylates

Table A.1. Acute Toxicity Profile of Alkyl Amine Polyalkoxylates

Guideline No.	Study Type	MRIDs #	Results	Toxicity Category
81-1	Acute Oral – rat	46902001	**MON 0818 (CAS 61791-26-2) Tallow, POE n=15** LD50 = ♂ 1436.7 mg/kg LD50 = ♀ 1315.1 mg/kg (reported as 1200 mg/kg)	III
81-1	Acute Oral – rat	ICI CTL	**ATMER® 163 (CAS 70955-14-5) C13-C15, POE n=2** LD50 = 1500 mg/kg	III
81-1	Acute Oral – rat	CIT	**Armoblen 557 (CAS 68213-26-3) Tallow, POE n=5/12** LD50 =1663 mg/kg	III
81-1	Acute Oral – rat	CPT	**Ethomeen C/12 (CAS 61791-31-9)** **Coco, POE 2** LD50 = 6600 mg/kg	IV
81-1	Acute Oral – rat	Safepharm	**Ethomeen C/15 (CAS 61791-14-8) Coco, POE n=5** LD50 >200 mg/kg	II
81-1	Acute Oral – rat	Safepharm	**Ethomeen T/12 (CAS 61791-44-4)** **Tallow, POE 2** LD50 = >2000 mg/kg	III
81-1	Acute Oral – rat	Safepharm	**Ethomeen S/12 (CAS 73246-96-5)** **Soya, POE 2** LD50 = 1260 mg/kg	III
81-2	Acute Dermal - rabbit	46902001	**MON 0818 (CAS 61791-26-2)** LD50 > 1260 mg/kg	II

Table A.1. Acute Toxicity Profile of Alkyl Amine Polyalkoxylates				
Guideline No.	**Study Type**	**MRIDs #**	**Results**	**Toxicity Category**
81-3	Acute Inhalation - rat	CIVO/TNO	**Armoblen 557 (CAS 68213-26-3)** LC50 (**4 hr**) 0.66 mg/L (0.42-0.85)	III
		Temple U	**Ethomeen C/12 (CAS 61791-31-9)** LC 50 (**1 hr**) 0.98 mg/L)	III
		Temple U	**Ethomeen T/12 (CAS 61791-44-4)** LC50 (**1 hr**) 3.19 mg/L	IV
81-4	Primary Eye Irritation Rabbit	46902001	**MON 0818 (CAS 61791-26-2)** Corrosive	I
		CIVO/TNO	**Armoblen 557 (CAS 68213-26-3)** Non-irritating/non-corrosive	
		Leberco Lab	**Ethomeen C/12 (CAS 61791-31-9)** Severely irritating (irreversible corneal opacity, iritis, redness, sewlling, discharge of conjunctiva (2 studies)	
		CPT	**Ethomeen T/12 (CAS 61791-44-4)** Corrosive	
		FDRL	**Ethomeen T/25 (CAS 61791-26-2)** Persistent extreme corneal opacity, iritis, necrosis of conjunctiva tissue (3 studies)	
		PSL	**Ethomeen T/30 (CAS 61791-26-2)** Corrosive	
		CPT	**Ethomeen T/25 (CAS 61791-26-2)** Persistent extreme corneal opacity, iritis, necrosis; corrosive	
			Ethomeen T/30 (CAS 61791-26-2) Corrosive	

Table A.1. Acute Toxicity Profile of Alkyl Amine Polyalkoxylates				
Guideline No.	**Study Type**	**MRIDs #**	**Results**	**Toxicity Category**
81-5	Primary Skin Irritation - rabbit	46902001	**MON 0818 (CAS 61791-26-2)** Severely irritating to skin	II
		EB0467	**ATMER® 163 CAS 70955-14-5** Corrosive (undiluted)	
		CIT	**Armoblen 557 (CAS 68213-26-3)** Non-irritant	
		Safepharm	**Ethomeen C/12 (CAS 61791-31-9)** Moderate to severe irritant (4 hr)	
		Safepharm	**Ethomeen C/12 (CAS 61791-31-9)** Moderate to severe irritant (4 hr)	
		IBR-US, Inc	**Ethomeen C/25 (CAS 61791-14-8)** Minimally irritating (4 hr)	
		Safepharm	**Ethomeen T/15 (CAS 61791-26-2)** Severely irritating but not corrosive (4 hr)	
81-6	Dermal Sensitization Guinea pig	46918001	**MON 0818 (CAS 61791-26-2)** Dermal sensitizer	
		Hill Top	**Ethomeen T/12 (CAS 61791-44-4)** Not a sensitizer	
		MB Lab	**Ethomeen T/12 (CAS 61791-44-4)** May be a sensitizer to sensitive individuals (mice)	

A.2. Toxicity Profile for the Alkyl Amine Polyalkoxylates

Table A.2. Toxicology Profile of the Alkyl Amine Polyalkoxylates

Guideline No./ Study Type	MRID No. (year)/ Classification /Doses	Results
870.3100 90-day/4-week oral toxicity SD rats **MON 0818** **CAS 61791-26-2 (tallow, POE 15))**	MRID 46918003C (90-day) 1990 MRID 46918002C (28-day) 1989 0, 500, 1500, 4500 ppm 0, 33/39.9, 99.3/123.1, 291.6/356.6 ♂/♀mg/kg/day Acceptable/guideline	NOAEL = 500 ppm (33/39.9 mg/kg/day) LOAEL = 1500 ppm (99.3/123.1 mg/kg/day, based on irritation in the intestines and colon (hypertrophy and vacoulation of histiocytes in lamina propria of jejunum and ileum and histiocytosis and accumulation of macrophage aggregates in mesenteric lymph nodes.
870.3100 4-week oral toxicity SD rats **MON 0818** **CAS 61791-26-2 (tallow, POE n=15)**	MRID 46918002C/46918002/ 47066302/47066302C (2006/2007) 0. 800, 2000, 5000 ppm (males 51.7, 122.8, 268.7 mg/kg/day; females 63.2, 159.9, 324.8 mg/kg/day) Acceptable/nonguideline (RF)	NOAEL = males 51.7 mg/kg/day LOAEL = males 122.8 mg/kg/day, based on reduced body weight gain and food consumption NOAEL = females 159.9 mg/kg/day LOAEL = females 324.8 mg/kg/day, based on reduced body weight, body-weight gain, food consumption, and irritation in the colon (soft stools).
870.3100 90-Day oral toxicity Sprague-Dawley (Crl:CD®BR) rats **AMTER® 163** **CAS 70955-14-5 (C13-C15, POE n=2)**	MRID 47041301 (1991) 0, 15, 30, or 150 mg/kg/day *via* gavage Acceptable/guideline	NOAEL = 15 mg/kg/day LOAEL = 30 mg/kg/day, based on increased mortality, salivation, and posterior subcapsular cataracts in males as well as wheezing, and macro- and microscopic changes in the nonglandular stomach of both sexes. 2 death @30 mg/kg/day (days 36, 78); 5 deaths @150 mg/kg/day (males days 56, 59, 78 and 82; female day 79) @150 mg/kg/day, males ↓BWG 30%/females 15%; wheezing & salivation from wk 2 on
870.3150 90-Day oral toxicity in nonrodents (beagles) **ATMER® 163** **CAS 70955-14-5 (C13-C15, POE n=2)**	MRID 47041302 (1991) 0, 15, 30, 100 mg/kg/day (capsules) Acceptable/nonguideline	NOAEL = 30 mg/kg/day LOAEL = 100 mg/kg/day, based on clinical signs (increased incidence of salivation, emesis, and soft feces (with mucus alone or mucus and bile-like material)) in males and females, increased alanine aminotransferase (ALT/SGPT) levels in females, and an increased incidence of pigment accumulation in the Kupffer cells and bile canaliculi in the livers of females.

Table A.2. Toxicology Profile of the Alkyl Amine Polyalkoxylates		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
870.3100 28-day oral toxicity CD rats **Armoblen 557** **CAS 68213-26-3 (Tallow, POE n=5/12)**	MRID 47193901 (1994) 0, 15, 75, or 200 mg/kg/day (gavage) Unacceptable (upgradeable)/guideline (% a.i.)	NOAEL = 75 mg/kg/day (males) LOAEL = 200 mg/kg/day, based on decreased body weight, body weight gain and food conversion efficiency in males; NOAEL = 200 mg/kg/day (females) HDT
870.3700a Prenatal developmental (Charles River Crl:CDBr female rats) **MON 0818** **CAS 61791-26-2 (tallow, POE n=15)**	MRID 46902005 (1990) 0 (corn oil), 15, 100, 300 mg/kg/day GD 6-15 (gavage) 71.9% a.i. Acceptable/guideline	Maternal NOAEL = 100 mg/kg/day Maternal LOAEL = 300 mg/kg/day, based on mortality, clinical signs (rales, soft stools, mucoid feces, diarrhea; females rales, yellow anogenital staining), and decreased body weight, body-weight gain, food consumption. Developmental toxicity NOAEL = 300 mg/kg/day, HDT
870.3800 (screening) Reproduction and fertility effects Crl:CD(SD) IGS BR Sprague-Dawley rats (10 weeks old at start) Screening study **(extended to two generations (↓ live litter size)** assessed gonadal function, mating behavior, conception, parturition, lactation of F0 and F12 generations; developmental of F1 (PND 70) and F2 (PND 4) generations **MON 0818** **CAS 61791-26-2 (tallow, POE n=15)**	MRID 47097401 (2007) 0, 100, 300, 1000 ppm (diet) males F0 (5.5, 16.6, 56.1)/ F1 (5.0, 14.9, 52.8) mg/kg/day females F0 (6.7, 19.5, 66.6)/ F1 (6.9, 18.9, 64.9) mg/kg/day 10 weeks prior to mating 69-73% a.i. Acceptable/nonguideline reproductive performance, fertility, mating performance, blood samples for testosterone &/or thyroid hormone conc. F1 (1/sex/litter @ necropsy); sperm evaluation (motility/morphology) F1 males; estrous cyclicity; litter size, viability, clinical signs, BW/BWG; developmental parameters (sexual & physical); macroscopic abnormalities @ necropsy (F1 & F2 pups)	Reproductive/offspring NOAEL = 300 ppm (F0/F1males 16.6/14.9; F0/F1 females 19.5/18.9 mg/kg/day Reproductive/offspring LOAEL =1000 ppm (F0/F1males 56.1/52.8; F0/F1 females 66.6/64.9 mg/kg/day, based on litter loss, increase mean number of unaccounted-for implantation sites and decreased mean number of pups born, live litter size and postnatal survival from birth to LD 4 (F1). At 1000 ppm, 3 F0 dams w/ small litters (2-4 pups/litter), and some of these pups died before PND 4; effect not repeated in F2 litters Systemic toxicity NOAEL = 1000 ppm (F0/F1males 56.1/52.8; P/F1 females 66.6/64.9 mg/kg/day, HDT

Table A.2. Toxicology Profile of the Alkyl Amine Polyalkoxylates		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
OECD 422 Crl:CD(SD) IGS BR rats **MON 0818** **CAS 61791-26-2 (tallow, POE n=15)** **MON 8109** **CAS 61791-31-9 (Coco, POE n=2)**	MRID 47405101 (2008) MON 8109: 0, 30, 100, 300, 2000 ppm (diet; administered for 14 days prior to mating until study termination) males: 0, 2, 8, 23, 134 mg/kg/day females: 0, 3, 9, 26, 148 mg/kg/day MON 0818: 1000 ppm (diet; administered for 14 days prior to mating until study termination) males: 0, 76 mg/kg/day females: 0, 86 mg/kg/day	MON 0818: parental toxicity/reproductive/ developmental NOAEL = 1000 ppm males 76 mg/kg/day; females 86 mg/kg/day. MON 8109: reproductive NOAEL = 2000 ppm (males 134 mg/kg/day; females (148 mg/kg/day) reproductive LOAEL was not demonstrated. MON 8109 parental toxicity NOAEL = 300 ppm (males 23 mg/kg/day; females 26 mg/kg/day) LOAEL = 2000 ppm (males 134 mg/kg/day; females: 148 mg/kg/day), based on clinical signs, decreased body weight and food consumption (both sexes) MON 8109 developmental toxicity NOAEL = 300 ppm (males 23 mg/kg/day; females 26 mg/kg/day) Developmental toxicity LOAEL = 2000 ppm (males 134 mg/kg/day; females 148 mg/kg/day, based on decreased postnatal survival, reduced live litter size on postnatal day 0, reduced number of pups born, and reduced number of implantation sites.. ***FOB and locomotor activity (recorded for 6 males/group nearend of study; 6 females/group on LD 4)*** no treatment-related effects reported on FOB or motor activity
Bacterial reverse mutation test 870.5100 **MON 59112** **No CAS#**	MRID 46914604 strains TA1535, TA1537, TA98 and TA100 of *Salmonella typhimurium* and strain WP2 *uvr*A of *Eschericha coli* 0, 1, 3.33, 10, 33.3, 100 or 333 µg/plate with and without S9 activation for the *Salmonella* strains and 0, 10, 33.3, 100, 333, 1000 or 3330 µg/plate +/-S9 for WP2 *uvr*A. Acceptable/guideline	No evidence of induced mutant colonies over background

Table A.2. Toxicology Profile of the Alkyl Amine Polyalkoxylates		
Guideline No./ Study Type	**MRID No. (year)/ Classification /Doses**	**Results**
Bacterial reverse mutation test 870.5100 **MON 0818** **CAS 61791-26-2 (tallow)**	MRID 46918004 strains TA1535, TA1537, TA98 and TA100 of *Salmonella typhimurium* (0.001, 0.003, 0.01, 0.03 or 0.1 mg/plate with S9 & 0.0003, 0.001, 0.003, 0.01 or 0.03 mg/plate without S9. repeat assay on TA1535 and TA1537 (± S9). cytotoxicity not observed; second cytotoxicity assay. Concentrations of MON 0818 ranging from 0.01 to 1.0 mg/plate +S9 and 0.003 to 0.3 mg/plate –S9 were tested in strain TA98; 0.001 to 0.10 mg/plate ±S9 in TA100; 0.001 to 0.1 mg/plate –S9 in TA1535; 0.003 to 0.3 mg/plate +S9 and 0.001 to 0.1 mg/plate –S9 in TA1537. Acceptable/guideline	MON 0818 was tested up to cytotoxic concentrations in all strains, but failed to induce a mutagenic response in this test system. The positive controls induced the expected mutagenic responses in the appropriate strain. **There was no evidence of induced mutant colonies over background.**
Mammalian erythrocyte micronucleus test 870. 5395 **MON 0818** **CAS 61791-26-2 (tallow)**	MRID 46902007 (1998) 100 mg/kg Acceptable/guideline	No significant increase in frequency of micronecleated polychromatic erythrocytes in bone marrow after any harvest time up to maximum tolerated dose.
Mammalian erythrocyte micronucleus test 870. 5395 **MON 59112** **No CAS#**	MRID 46930503 (2000) 0, 375, 750 or 1500 mg/kg male mice;0, 500, 1000 or 2000 mg/kg female mice Acceptable/guideline	No significant increase in the frequency of MPCEs in any treatment group at either harvest time

A.3. Toxicity Study Executive Summaries

Subchronic repeat dose toxicity studies

EXECUTIVE SUMMARY: In a 90-day oral toxicity study (MRID 46918003), MON 0818 (71.9% a.i., Lot No. PIT-8907-757-1) was administered in the diet *ad libitum* to three groups of 10 male and 10 female Sprague-Dawley rats for 90 days. Target test diet concentrations were 500, 1500, or 4500 ppm (equivalent to 33.0, 99.3, 291.6 mg/kg

bw/day in males and 39.9, 123.1, and 356.6 mg/kg bw/day in females). A similar concurrent control group of rats received basal diet only. Doses were selected based on a previous 28-day range-finding study (MRID 46918002C).

Exposure to MON 0818 in the diet at the mid- and high-dose levels of 1500 and 4500 ppm resulted in statistically- and toxicologically-significant effects. Toxicity observed at 4500 ppm consists of clinical signs (soft stools, 3 incidences in 2 males and 86 incidences in all females) observed from day 16 through day 92 of the study, decreased mean body weights throughout the study (ranging from 12-20% and 8-18% in males and females, respectively), and decreased mean total body weight gains in males (31%) and females (35%). Food consumption was also significantly reduced throughout most of the study (13 weeks for males and 10 weeks for females), particularly during the first week of the study (32% decrease in males and 27% decrease in females). Since a food efficiency assessment was not conducted, it is not possible to determine if the decreases in body weights, body weight gains, and food consumption were due, in part, to the unpalatability of the diet. Statistically-significant changes in hematological parameters observed in females may be a result of the inflammation observed in the intestines. Statistically-significant changes in clinical chemistry parameters and organ weights observed in high-dose males and females are likely a result of decreased food consumption/nutrient absorption and body weight.

At both the 1500 and 4500 ppm dose levels, microscopic examination conducted at necropsy revealed lesions, including: (1) hypertrophy and/or vacuolation of histiocytes in the lamina propria of the ileum in all high-dose males and females, and 4 of 10 mid-dose males and 4 of 10 mid-dose females; (2) hypertrophy and/or vacuolation of histiocytes in the lamina propria of the jejunum in 4 of 10 high-dose males, 7 of 10 high-dose females, and 1 mid-dose female; and (3) sinus histiocytosis in 9 of 10 high-dose males, 6 of 10 high-dose females, and 2 of 10 mid-dose males and females; and (4) accumulation of macrophage aggregates in the cortex and medullary cords of the mesenteric lymph node in 8 of 10 high-dose males, 7 of 10 high-dose females, and 2 of 10 mid-dose females. These inflammatory changes are likely the cause of the soft stools observed during the study and are considered treatment-related.

No statistically-significant treatment related effects on body weight, body weight gain, food consumption, hematological/clinical chemistry parameters, and organ weights were observed at the low-dose level of 500 ppm. In addition, no gross abnormalities or histopathological findings related to treatment were observed at this dose level.

Based on review of the study, the no-observable-adverse-effect-level (NOAEL) for MON 0818 is 500 ppm (33.0 mg/kg bw/day in males and 39.9 mg/kg bw/day in females). The lowest-observable-adverse-effect-level (LOAEL) is 1500 ppm (99.3 mg/kg/day in males and 123.1 mg/kg bw/day in females), based on irritation in the intestines and colon (hypertrophy and vacuolation of histiocytes in the lamina propria of the jejunum and ileum, and histiocytosis and accumulation of macrophage aggregates in the mesenteric lymph nodes).

This study is classified as **Acceptable/Guideline** and satisfies the guideline requirement for a 90-day oral toxicity study in rodents (OPPTS 870.3100).

EXECUTIVE SUMMARY: In a 90-day oral gavage toxicity study (MRID 47041301), ATMER® 163 (100% a.i.; batch/lot # not reported) was administered to 20 Sprague-Dawley (Crl:CD®BR) rats/sex/dose at concentrations of 0, 15, 30 or 150 mg/kg bw/day. Deionized water was administered to controls.

There were no toxicologically significant compound-related effects based on the assessment of clinical chemistry and the limited assessment of organ weights. Urinalysis was not done.

Numerous clinical signs were observed in animals dosed at 150 mg/kg bw/day. The most notable signs were wheezing and salivation, which were seen from all animals and in some animals treated with 30 mg/kg bw/day. Other clinical signs observed in both sexes dosed at 150 mg/kg bw/day included blood crust and/or red discharge (nose), dyspnea, rhinorrhea, opaque eyes, redness, hunched posture, thin, urine stains, rough haircoat, desquamation and an increased incidence of alopecia. Two males treated with 30 mg/kg bw/day, as well as four males and one female treated with 150 mg/kg bw/day, died during the study. Statistically significant body weight and body weight gain deficits were observed in both sexes dosed at 150 mg/kg bw/day; overall body weight gains were 30.5% and 15.3% lower than control values in males and females, respectively. Statistically significant decreased food consumption was seen at 150 mg/kg bw/day in males only. The ophthalmoscopic assessment revealed posterior subcapsular cataracts in males at 30 and 150 mg/kg bw/day and in females at 150 mg/kg bw/day while complete cataracts were found only at 150 mg/kg bw/day in both sexes. Increased mean values for platelet count, white blood cell count, segmented neutrophil count and lymphocyte count were seen at the 150 mg/kg bw/day dose in both males and females; all of the increases were statistically significant except the increased lymphocyte count in males. These findings are often associated with tissue inflammation. Inflammation and other relevant findings were observed in the lungs and stomach of both sexes at this dosage. The only noteworthy compound-related gross pathology findings were in the nonglandular stomach and eyes. The findings in the nonglandular stomach, desquamation and alteration of mucosa, were found primarily in males and females dosed at 150 mg/kg bw/day, however, some alterations of mucosa were also seen in animals dosed at 30 mg/kg bw/day. Opaque eyes, which were seen in both sexes at 150 mg/kg bw/day were consistent with the ophthalmoscopic findings of complete cataracts. Compound-related histopathologic findings included inflammation in the lungs of males and females dosed at 150 mg/kg bw/day and the nonglandular stomach of males and females dosed at 30 and 150 mg/kg bw/day. The inflammation in lungs might have been associated with inadvertent aspiration since previous studies have established that ATMER® 163 is a primary irritant. Dose-related incidences of acanthosis in the nonglandular stomach were seen in males and females dosed at 30 and 150 mg/kg bw/day. The only noteworthy finding in the glandular stomach was suppurative inflammation at terminal sacrifice in two females dosed at 150 mg/kg bw/day. Additionally, the microscopic assessment

showed cataracts in the eyes of both sexes dosed at 150 mg/kg bw/day; most were bilateral.

The LOAEL for ATMER® 163 in Sprague Dawley rats in this study is 30 mg/kg bw/day based on increased mortality, salivation, and posterior subcapsular cataracts in males as well as wheezing, and macro- and microscopic changes in the nonglandular stomach of both sexes. The NOAEL is 15 mg/kg bw/day.

Although there were several deficiencies (See Study/Report Deficiencies), this 90-day oral toxicity study in rats is **Acceptable/Guideline** and satisfies the guideline requirement for a 90-day oral toxicity study (OPPTS 870.3100; OECD 408) in a rodent species. Although several guideline-recommended organs were not weighed, there were no compound-related gross or histopathologic changes observed in the omitted organs.

EXECUTIVE SUMMARY: In a subchronic (90-day) oral toxicity study (MRID 47041302), ATMER® 163 (100% a.i.; batch/lot# not provided) was administered *via* capsule to three groups of 4 male and 4 female beagle dogs for 13 weeks at dose levels of 15, 30, or 100 mg/kg bw/day. A similar concurrent control group of dogs received empty capsules only. There were no unscheduled deaths during the study. All dogs survived until termination.

Exposure to ATMER® 163 *via* capsules at the high-dose level of 100 mg/kg bw/day resulted in statistically- and toxicologically-significant effects. Toxicity observed at 100 mg/kg bw/day included the clinical signs of increased incidence of salivation, emesis, and soft feces (noted with mucus alone or mucus and bile-like material). Salivation was observed in all of the males and females beginning during week 3 of the study (6 of the 8 animals) and continuing over a period of 5 to 11 weeks. Emesis was also observed in all of the males and females and was first observed during the first two weeks of the study in 7 of the 8 animals and continued over a period of 1 to 11 weeks. Soft feces (mucoid) were observed in 3 of the 4 males and in all of the females over a period of 2-7 weeks; soft feces (mucoid/bilious) were observed in the high-dose animals (3 males and 2 females) over a period of 1-3 weeks. All of these clinical signs are considered treatment-related based on the high frequency of occurrence and clear dose-response relationship. In addition, mean alanine aminotransferase (ALT/SGPT) levels were significantly increased (154%), relative to controls, in females. Microscopic examination conducted at necropsy revealed an increased in pigment accumulation in the Kupffer cells and bile canaliculi in the livers of all females. The increased pigment accumulation was not observed in any of the treated males or in the low- and mid-dose females. Other microscopic findings were observed, but are not dose-related or are found in control animals as well as treated animals.

The statistically-significant increase (22%) in mean red blood cell (RBC) counts, relative to controls, observed in high-dose females was within the historical control range. The significant increases (6%) in mean calcium levels observed in the mid- and high-dose females were small in magnitude, and the observed significant decrease (23%) in mean

blood urea nitrogen (BUN) levels in the mid-dose males did not follow a dose response pattern. All of the changes are considered to be incidental to treatment.

No statistically-significant effects on body weight, body weight gain, food consumption, or organ weights were observed at any dose level. In addition no gross abnormalities or ophthalmological changes related to treatment were observed.

Based on review of the study, the no-observable-adverse-effect level (NOAEL) for ATMER® 163 is 30 mg/kg bw/day. The lowest-observable-adverse-effects-level (LOAEL) is 100 mg/kg bw/day, based on clinical signs (increased incidence of salivation, emesis, and soft feces (with mucus alone or mucus and bile-like material)) in males and females, increased alanine aminotransferase (ALT/SGPT) levels in females, and an increased incidence of pigment accumulation in the Kupffer cells and bile canaliculi in the livers of females.

This study is classified as **Acceptable/Nonguideline** and does satisfy the guideline requirement for a 90-day oral toxicity study in nonrodents (OPPTS 870.3150).

EXECUTIVE SUMMARY: In a four-week oral toxicity study (MRID 47193901), Armoblen 557 (a.i. not provided, Batch No. B.31401-1) was administered daily by gavage to groups of five male and five female CD rats at concentrations of 0, 15, 75, or 200 mg/kg bw/day.

All rats survived until scheduled termination. Salivation in males and females at 75 and 200 mg/kg bw/day was probably due to the taste of the test material and was not considered toxicologically significant. Noisy respiration reported in 1-3 females receiving 200 mg/kg bw/day was not associated with postmortem effects and therefore, was not considered toxicologically significant. Brown staining around the muzzle observed occasionally in females at 75 mg/kg bw/day and males and females at 200 mg/kg bw/day was not considered toxicologically significant. Mean body weight was decreased in males (11-17% lower than controls) and females (4-7% lower than controls) at 200 mg/kg bw/day. The overall bodyweight gain was decreased in males receiving 75 mg/kg bw/day (13% lower than controls) and in males and females receiving 200 mg/kg bw/day (27% and 14% lower than controls, respectively). Overall food consumption for females receiving 200 mg/kg bw/day was decreased (10% lower than control). Food consumption was decreased in males at 200 mg/kg bw/day during Week 1 only. The overall food conversion efficiency was decreased in males at 75 and 200 mg/kg bw/day (13 and 23% lower than controls, respectively).

Alterations in hematology and clinical chemistry parameters were either not treatment-related or not toxicologically significant. Increases in the absolute and relative adrenal weights in males and females at 200 mg/kg bw/day were not accompanied by microscopic findings and were not considered toxicologically significant.

Based on decreased body weight, body weight gain and food conversion efficiency, a LOAEL of 200 mg/kg bw/day for Armoblen 557 in male CD rats was established; the NOAEL in male CD rats was 75 mg/kg bw/day. A LOAEL for Armoblen 557 in female CD rats was not established. The NOAEL in female CD rats was 200 mg/kg bw/day.

This 28-day oral toxicity study in the rat is **Unacceptable/Guideline/Upgradeable** and does not satisfy the guideline requirement for a repeat dose 28-day oral toxicity study (OPPTS 870.3050; OECD 407) in rats. The study may be upgraded to acceptable with submission of the percent active ingredient used for the study.

EXECUTIVE SUMMARY: In a 28-day oral toxicity study (MRID 46918002C), MON 0818 (70.6% a.i.; Lot XLI-320 [MRID 46918002]) was administered to groups of ten Sprague-Dawley rats/sex/dose in the diet at dose levels of 0, 800, 2000, and 5000 ppm (0, 51.7, 122.8, and 268.7 mg/kg bw/day for males, respectively, and 0, 63.2, 159.9, and 324.8 mg/kg bw/day for females, respectively). Males and females were sacrificed on Days 28 and 29, respectively, and subjected to gross necropsy.

All rats survived until scheduled termination. No significant treatment-related effects were found at 800 ppm of MON 08189 in the diet. When fed a diet containing 2000 ppm of MON 0818, toxicity was evident in male rats over the first eight days of the study as a reduction in body weight gain (-62%), food consumption (-18% g/kg bw/day), and food efficiency (-80%). The male rats were not able to recover by the end of the study, with overall body weight gain reduced 34% relative to controls. No effects on body weight were observed in females fed 2000 ppm.

Dietary exposure to 5000 ppm resulted in toxicity as indicated by reduced body weight, body weight gain, food consumption, and food efficiency in males and females, and irritation of the colon, particularly in females. Mean average body weight in males and females was reduced by 15-19% and 10-13% of controls, respectively, with terminal body weight reduced by 23% and 15%, respectively. Body weight gain was most severely affected during the first week of dosing, with body weight gain in males and females reduced by 183% and 455% of controls, respectively; overall body weight gain (Days 1-28/29) was significantly reduced by 89% and 102%, respectively. Food consumption (g/day) was statistically reduced at all dosing intervals in males and females. When corrected for body weight, food consumption (g/kg bw/day) was reduced in males over days 1-8 and 8-16 by 51% and 11%, respectively, and in females on Days 1-8 by 48% and over the entire dosing period of Days 1-29 by 11%. Food efficiency was statistically decreased over Days 1-8 in high-dose males and females by 315% and 1091%, respectively, and increased in high-dose females on Days 16-22 by 131%. Irritation of the colon was evidenced as an increased incidence of soft stool in both sexes (3/10 males affected a total of 4 times; 8/10 females affected 24 times), and pathological findings of prominent/enlarged lymphoid aggregates in the colon of 5 of 10 treated females.

Based on reduced body weight gain and food consumption in mid-dose male rats, a LOAEL of 2000 ppm for MON 0818 (122.8 mg/kg bw/day) was established. The NOAEL was 800 ppm (51.7 mg/kg bw/day) for males. A LOAEL of 5000 ppm for MON 0818 (324.8 mg/kg bw/day) was established for female Sprague Dawley rats based on reduced body weight, body weight gain, food consumption, and irritation in the colon. The corresponding NOAEL for female rats was 2000 ppm (159.9 mg/kg bw/day).

This 28-day oral toxicity study in the rat is **Acceptable/Non-guideline** and does not satisfy the guideline requirement for a repeat dose 28-day oral toxicity study (OPPTS 870.3050; OECD 407). The study had a number of deficiencies, including lack of analyses of the concentration, stability, and homogeneity of the test material in the diet; no hematology or clinical chemistry analyses were performed; no rationale for dose selection was provided; and a full microscopic examination was not conducted on control and high-dose animals. These deficiencies did not compromise the integrity of the study, however, in that the study was designed to set dose levels for a subsequent 90-day oral rat study (MRID 46918003C).

Developmental/Reproduction Toxicity Studies

EXECUTIVE SUMMARY: In a developmental toxicity study (MRID 46902005), MON 0818 (71.9 % a.i., Lot No. PIT-8907-7571) was administered in Mazola® Corn Oil to 25 Charles River Crl:CDBr female rats/dose by gavage at dose levels of 0 (corn oil only), 15, 100 or 300 mg/kg bw/day from days 6 through 15 of gestation. On day 20 of gestation, all surviving females were sacrificed for a scheduled Cesarean section. Developmental parameters observed and noted included: number of viable fetuses, early and late resorptions, total implantations, total corpora lutea, sex and weight of fetuses and external, visceral and skeletal examinations of all fetuses.

Six of the twenty-five high-dose females died during gestation days (GD) 8-13 (2 on GD 8; 1 on GD 10 and GD 11, and 2 on GD13). Clinical signs were also observed in the high-dose females and included: rales (12/25), labored respiration (3/25), yellow uro- (15/25) or anogenital (14/25) matting and mucoid feces (22/25) compared to none of the control animals. Few to no clinical signs were observed in the mid-dose and low-dose females. High-dose females weighed significantly ($p<0.01$) less than the controls from study day 9 until sacrifice at study day 20. High dose females also gained 59% less weight compared to controls during treatment (days 6-16). Body weight was similar to controls in the low- and mid-dose groups. Gravid uterine weight was not affected by treatment in any of the groups. High-dose females ate statistically ($p < 0.01$) less food compared to the control rats with the most significant decrease (55% less than controls) on days 6-9 before gradually improving to become comparable to controls by day 16. Overall for days 6-16, the high-dose group ate 29% less than the controls. Food consumption for the low-dose and mid-dose females was comparable to that of controls throughout the study, except for days 6-9 when the mid-dose group had a statistically

significant ($p<0.05$) decrease. There were no treatment-related effects observed on liver weight or gross pathology at necropsy in any of the treated dams.

The maternal lowest-observed-adverse-effect level (LOAEL) for MON 0818 in rats is 300 mg/kg bw/day, based on increased mortality, clinical signs, and decreased body weight, body weight gain, and food consumption. The maternal no-observed-adverse-effect level (NOAEL) for MON 0818 is 100 mg/kg bw/day.

No treatment-related differences were observed in the mean number of corpora lutea, implantations, live fetuses or resorptions. Mean fetal weight was not affected by maternal treatment with the test article. The mean number of malformations on external examination of the fetuses from the high-dose dams appeared to be high but most were observed in a single one fetus and a dose response was not observed. On visceral examination, in the high-dose group, one fetus was missing a urinary bladder, one fetus had stenosis of the right carotid artery and two fetuses had situs inversus. One control fetus also had situs inversus. These were not considered treatment-related as there was not a dose response for the situs inversus and the others were within the historical control data range. Vertebral anomalies with or with/out rib anomalies were observed in one fetus in the high-dose group but this was within the range of historical control data. No malformations were observed in the low- or mid-dose groups. Several skeletal variations in the sternebrae and ribs were identified but they were observed in both the control and treated groups at similar incidences and are not considered treatment-related.

The developmental lowest-observed-adverse-effect level (LOAEL) for MON 0818 in rats could not be determined as no effects were associated with treatment. The developmental no-observed-adverse-effect level (NOAEL) for MON 0818 is 300 mg/kg bw/day.

The developmental toxicity study in the rat is classified **acceptable/Guideline** and **satisfies** the guideline requirement for a developmental toxicity study (OPPTS 870.3700; OECD 414) in the rat.

EXECUTIVE SUMMARY: In a screening study (MRID 47097401), the potential reproductive toxicity and developmental (prenatal and postnatal) toxicity of the test article, MON 0818 (69-73% a.i.; Lot# GLP-0309-14324-I), was evaluated in CD (Sprague-Dawley) rats through two successive generations. The study was designed to evaluate the effects of MON 0818 on male and female reproduction within the scope of a screening study. The study was extended to a two-generation study when a decrease in live litter size was observed at the high-dose level. In the study, MON 0818 was administered orally via the diet to three groups of 20 male and 20 female CD rats. Target test diet concentrations were 100, 300 or 1000 ppm. A similar concurrent control group of rats received basal diet only. At approximately 10 weeks of age, the P animals were dosed via diet for at least 70 days prior to mating and continuing to sacrifice (males) or LD 21 (females). All P adults were sacrificed following selection of the F_1 generation on PND 21.

Selection of parents for the F_1 generation was made from the weaned F_1 litters. Between PND 21 or 22 and 70, the weanling F_1 animals (3/sex/litter, if possible) were administered the test diet on a mg/kg basis (so not to overexpose the rapidly growing F_1 animals) at target concentrations of 0, 6, 18, or 61 mg/kg/day for the F_1 males and 0, 7, 22, or 74 mg/kg/day for the F_1 females. Beginning on PND 70, the F_1 animals selected for breeding from the control and high-dose groups only (2/sex/litter) were administered the test diet at a constant concentration (0 or 1000 ppm) for a minimum of 80 to 88 days prior to mating. The selected F_1 males continued to receive the test diet throughout mating and continuing until sacrifice (after the F_2 pups reached LD 4). The selected F_1 females continued to receive the test diet throughout mating, gestation and lactation and until the day of sacrifice (after the F_2 pups reached LD 4).

Mortality and clinical signs, body weights, body weight gains, food consumption, reproductive function, fertility and mating performance, absolute and relative organ weights, macroscopic abnormalities at necropsy, and histopathological findings were recorded for all parental/adult animals. In addition, blood samples for testosterone and/or thyroid hormone concentration determinations were collected from one F_1 male and one F_1 female per litter at the scheduled necropsy. Sperm evaluation (motility and morphology) was also performed on all F_1 male animals at termination. Litter size, viability, clinical signs, body weights, body weight gains, developmental (sexual and physical) parameters, and macroscopic abnormalities at necropsy were recorded for the F_1 and F_2 pups.

Survival and clinical conditions, mean body weights and food consumption (pre-mating, gestation, and lactation), reproductive performance, mean organ weights, and macroscopic and microscopic morphology of the P and F_1 parental generations were unaffected by administration of MON 0818 at all dose levels. Treatment-related effects were also not seen in estrous cyclicity, spermatogenic endpoints and testosterone and thyroid hormone levels of the F_1 generation or in the clinical signs, mean body weights, and developmental landmarks of the F_1 and F_2 pups, as well as the litter viability and postnatal survival of the F_2 litters.

Potential treatment-related effects were observed in litter loss, increased mean number of unaccounted-for implantation sites, and decreased mean number of pups born, live litter size and postnatal survival from birth to LD 4 in the high-dose P females and F_1 litters. These effects were limited to a small number of litters, not always statistically-significant, and were not reproduced in the F_2 litters. However, the increased (statistically-significant) mean number of unaccounted-for implantation sites exceeded the maximum mean value in the laboratory historical control data. While not statistically-significant, the corresponding reduced number of pups born and live litter size, as well as the reduced postnatal survival, were at or below the limits observed in the laboratory historical control data.

Therefore, the lowest-observed-adverse-effect level (LOAEL) for parental reproductive toxicity (P) and offspring developmental/neonatal toxicity (F_1) is 1000

ppm (56.1 and 52.8 mg product/kg/day (equivalent to 41 and 38.5 mg/kg/day) for the P and F_1 males, respectively, and 66.6 and 64.9 mg product/kg/day (equivalent to 48.6 and 47 mg/kg/day) for P and F_1 females, respectively), based on litter loss, increase mean number of unaccounted-for implantation sites and decreased mean number of pups born, live litter size and postnatal survival from birth to LD 4. The no-observed-adverse-effect level (NOAEL) is 300 ppm (16.6 and 14.9 mg product /kg/day (equivalent to 12 and 11 mg/kg/day) for the P and F_1 males, respectively, and 19.5 and 18.9 mg product/kg/day (equivalent to 14 and 13.7 mg/kg/day) for the P and F_1 females, respectively). The NOAEL for parental (P and F_1) systemic toxicity is 1000 ppm. A LOAEL for parental systemic toxicity was not determined.

This study is classified as **Acceptable-Nonguideline.** The study was conducted as an extended screening study. It does not fully satisfy the requirements for a two-generation reproductive study (OPPTS 870.3800) in rats because: (1) the test substance was not administered to the F_1 offspring until the F_2 generation was weaned; (2) only the F_1 males and females from the control and high-dose group were selected for breeding; (3) the P generation did not contain a sufficient number of mating pairs to yield at least 20 pregnant females; and, (4) spermatogenic endpoints were only assessed for F_1 males.

EXECUTIVE SUMMARY: In a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (MRID 47405101) MON 8109 (100% a.i., Lot # GLP-0611-17816-I) or MON 0818 (100% a.i., Lot # GLP-0609-17646-I) was administered to 12 Crl:CD(SD) rats/sex/dose in the diet at dose levels of 0, 30, 100, 300, or 2000 ppm MON 8109 (males 0, 2, 8, 23, 134 mg/kg/day; females 0, 3, 9, 26, 148 mg/kg/day) or 1000 ppm MON 0818 (males 76 mg/kg/day; females 86 mg/kg/day) for 14 consecutive days prior to mating (both sexes) and throughout gestation and lactation day 4 (females). Males received the test or basal diets for a total of 71-72 days, and the females received the test or basal diets for a total of 69-72 days. Functional observational battery (FOB) and locomotor activity data were recorded for 6 males/group near the end of diet administration and for 6 females/group on lactation day 4. Parental animals were sacrificed approximately 2.5 weeks after lactation day 4, and offspring were sacrificed on lactation day 4.

No mortality related to MON 8109 exposure occurred. Increased incidences of red material around the nose, reddened nose, and reddened mouth were test substance-related findings in males and females treated with 2000 ppm MON 8109. Mean body weight losses were noted at 2000 ppm MON 8109 in male and females during the first week of test diet administration. Lower mean body weight (8-12%) and/or body weight gain (males 37%; females 17%) with corresponding reduction in food consumption were observed in the animals from this group throughout the study. Male at the 2000 ppm MON 8109 dose level displayed decreased liver, kidney, thyroid, and heart weights, which can be attributed to the reduction in body weight. The females from this group had a lower number of implantation sites and lower live litter size. Offspring of these females had lower postnatal survival on PND0, PND0-1, PND1-4, and birth to PND4 compared to the control group. No effect of treatment was observed in male and female mating and fertility, male copulation and female conception indices, gestation length, functional

observational battery, locomotor activity, hematology, or serum chemistry. No test substance-related findings were noted in the 30, 100, or 300 ppm MON 8109 group males, females, or offspring.

No mortality related to MON 0818 exposure occurred. One female in the 1000 ppm MON 0818 group was found dead with dystocia on lactation day 1 and another was euthanized *in extremis* on gestation day 30 and found to have a ruptured uterus. No treatment-related effects were observed in male and female mating and fertility, male copulation and female conception indices, gestation length, functional observational battery, locomotor activity, hematology, or serum chemistry following exposure to 1000 ppm MON 0818.

The parental systemic LOAEL is 2000 ppm MON 8109 (134 mg/kg bw/day in males, 148 mg/kg bw/day in females), based on clinical findings, decreased mean body weight and body weight gain, and food consumption. The parental systemic NOAEL is 300 ppm MON 8109 (23 mg/kg bw/day in males, 26 mg/kg bw/day in females).

The developmental LOAEL is 2000 ppm MON 8109 (134 mg/kg bw/day in males, 148 mg/kg bw/day in females), based on decreased postnatal survival, decreased live litter size on postnatal day 0, reduced number of pups born, and reduced number of implantation sites. The developmental NOAEL is 300 ppm MON 8109 (23 mg/kg bw/day in males, 26 mg/kg bw/day in females).

A reproductive LOAEL for MON 8109 was not demonstrated. The reproductive NOAEL is 2000 ppm MON 8109 (134 mg/kg bw/day in males, 148 mg/kg bw/day in females).

A parental LOAEL for MON 0818 was not demonstrated. The parental NOAEL is 1000 ppm MON 0818 (76 mg/kg bw/day in males, and 86 mg/kg bw/day in females).

The reproductive/developmental toxicity LOAEL for MON 0818 was not demonstrated in this study. The reproductive/developmental toxicity NOAEL is 1000 ppm MON 0818 (76 mg/kg bw/day in males, and 86 mg/kg bw/day in females).

This study is **acceptable (guideline)** and satisfies the guideline requirement for a Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OECD 422) in the rat for MON 8109 and MON 0818 (limit test).

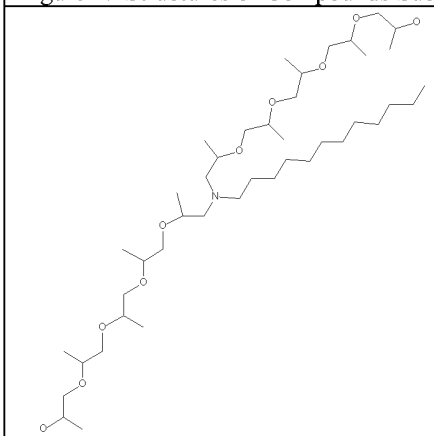
APPENDIX B

B.1. Structure-Activity Relationship (SAR) Discussion

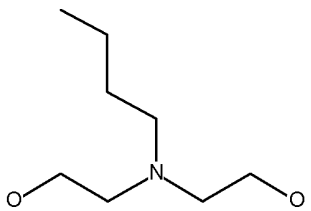
HED used DEREK for Windows (V. 11) to assess the potential toxicity of compounds in the inerts mixture. The products in this cluster are complex mixtures with compounds similar in structure, but of various carbon chain lengths. Therefore two compounds were

subjected to the DEREK analysis: one compound that represented a larger molecule expected in the mixture, and a small molecule that represents a potential environmental degradate, based on the postulated environmental degradation pathway. These compounds were selected on the basis that potential toxicity of intermediate-sized chemicals will be represented by the large and small chemicals selected. The structures are shown in Figure 1 below.

Figure 1. Structures of Compounds Subjected to Structure-Activity Analysis



Example large molecule



Example Postulated Environmental Degradate

Derek for Windows (LHASA Ltd.) is an expert system for the prediction of toxicity. It relies on a knowledge base of structural alerts and rules developed by scientists. When a test compound is inputted into the program, Derek for Windows scans the test compound for structural alerts contained within its database that are associated with specific toxicological endpoints and applies a series of reasoning rules to determine the likelihood of toxicity for the test compound. Information is provided on the rules used to make the prediction, along with descriptions of structural alerts identified, comments, available example compounds linked to the alerts and literature references.

DEREK did not identify any structural alerts of concern for the larger molecule tested, and a single respiratory irritation alert was identified for the smaller molecule. The respiratory irritation alert is expected for small amine molecules, which are known to be irritating. DEREK has developed more alerts for genotoxicity and carcinogenicity than other endpoints in the system. Considering what is already known about these specific compounds and other long-chain fatty acid compounds, along with the lack of structural alerts for carcinogenicity, chronic toxicity, or genotoxicity, HED has no specific concerns regarding chronic exposures other than those identified in the subchronic toxicity studies for this cluster.

APPENDIX C

C.1. Drinking Water Surrogate Analysis

Summary of Drinking Water Estimates of Four Surrogate Inert Chemicals

Notes:

1. Used a North Carolina cotton scenario with application date on July 1. This scenario should be a good representative of the numbers that you can expect from EFED. Also tried manipulation of application dates and weather files to ensure that there are no aberrations; these values look good in that regard.

2. PCA factors were not applied, but the impact of applying such factors (i.e., 0.5 to 0.9) would be insignificant in comparison to the vast uncertainties surrounding generation of concentrations from surrogate chemicals as well as uncertainties regarding the actual timing of applications.

3. All simulations were made at approximately 1 lb/A. Concentrations resulting from other application rates will be directly proportional to the application rate.

4. Table 1 gives the normalized concentration estimates for the case where all mass is applied on a single day. This should be the most conservative case.

5. Table 2 gives the normalized concentration estimates for the case where mass is distributed evenly over a 100-day period (April to June).

6. A range of degradation rates were used because degradation information was not available. 3 simulations were made 1) chemically stable in water and soil, 2) a 100 day half life in water and soil, and 3) a 10-day half life in water and soil. This should cover degradation.

7. Table 3 gives the chemical inputs used in the simulations.

Table 1. DW concentration for application lumped on a single day. (This maximizes the acute concentrations.) All concentrations are normalized to a yearly application of 1 kg/hA (1.12 lb/acre).

	Chemical 1	Chemical 2	Chemical 3	Chemical 4
Estimates based on Stable Assumption				
Acute (ppb)	1.1	41	33	0.005
Chronic	0.69	15	19	0.003
Cancer	0.47	12	15	0.002
Estimates based on assumption of a 100-day half life in soil and water				
Acute (ppb)	0.74	36	22	0.003
Chronic	0.33	8.8	7.7	0.002
Cancer	0.25	6.4	6.4	0.001
Estimates based on assumption of a 10-day half life in soil and water				
Acute (ppb)	0.48	25	15	0.002
Chronic	0.04	1.1	0.96	0.0002
Cancer	0.03	0.65	0.60	0.0002

Table 2. DW concentration for applications spread out over a 100-day period. This simulates a more even distribution of pesticide over the growing season. All concentrations are normalized to a yearly application of 1 kg/hA (1.12 lb/acre).

	Chemical 1	Chemical 2	Chemical 3	Chemical 4
Spread Out Values				
Estimates based on Stable Assumption				
Acute (ppb)	0.98	29	28	0.004
Chronic	0.70	13	18	0.003
Cancer	0.48	10	15	0.002
Estimates based on assumption of a 100-day half life in soil and water				
	0.57	21	17	0.003
	0.36	6.9	7.2	0.002
	0.27	5.3	6.4	0.001

	Chemical 1	Chemical 2	Chemical 3	Chemical 4
Estimates based on assumption of a 10-day half life in soil and water				
	0.16	7.8	4.3	0.001
	0.04	0.79	0.77	0.0002
	0.03	0.61	0.63	0.0002

Table 3 Chemical Inputs used in Simulations.

	Chemical 1	Chemical 2	Chemical 3	Chemical 4
Chemical Inputs:				
MW	*928*	*274*	*302*	*1185*
Solubility (mg/L)	*382*	*299*	*19.5*	*6.69e-8*
V.P. (mmHg)	*5.8e-27*	*1.76e-8*	*3.86e-8*	*3.77e-33*
Koc (ml/g)	*9.44e6*	*152*	*1345*	*2.57e9*

APPENDIX D

D.1. Listing of the Surrogate Active Ingredients

Table D.1. Listing of the 57 "Significant" Surrogate Active Ingredients

Insecticides (22)	Herbicides (20)	Fungicides (15)
Acephate	Acetochlor	Azoxystrobin
Aldicarb	Alachlor	Benomyl
Azinphos-methyl	Atrazine	Captan
Bifenthrin	Bentazon	Chlorothalonil
Carbaryl	Cyanazine (no food uses registered)	Fenarimol
Chlorpyrifos	Dicamba	Fosetyl-Al
Cryolite	Dimethenamid	Iprodione
Diazinon	Diuron	Mancozeb
Dimethoate	EPTC	Maneb
Endosulfan	Ethafluralin	Mefenoxam
Ethion	Fluometuron (registered on cotton only)	Metiram
Imidacloprid	Glyphosate	Tetraconazole
Lambda-Cyhalothrin	MCPA	Thiram
Methamid	Metolachlor	Thiophanate-methyl
Methomyl	Molinate (no food uses registered)	Ziram
Methyl Parathion	Pendimethalin	
Oxydemeton-methyl	Propanil	
Permethrin	Simazine	
Phorate	Trifluralin	
Phosmet	2,4-D	
Propargite		
Terbufos		

APPENDIX E

E.1. Residential Exposure Assessment Introduction

This document is a summary of the methods used to calculate residential exposures to the JITF inert cluster inert ingredients. These methods and a basic description of how they are used were taken from References A and B [available at the end of Appendix E]. These references also contain more detailed information on the rationale behind these methods. Only those methods pertinent to the JITF inert cluster inert ingredients exposures are discussed in this document.

Tasks associated with residential pesticide handlers are categorized using one of the following terms:

- Mixers and/or Loaders: these individuals perform tasks in preparation for an application. For example, mixers/loaders would mix and prepare the product prior to application.
- Mixer/Loader/Applicators and or Loader/Applicators: these individuals are involved in the entire pesticide application process (they do all job functions related to a pesticide application event). These individuals would perform the mix/load function, transfer the product (containing the inert) into the application equipment, and then complete the product application.

A chemical can produce different effects based on how long a person is exposed, how frequently exposures occur, and the level of exposure. HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. HED completes both short- and intermediate-term assessments for residential scenarios in all cases because these kinds of exposures are likely and acceptable use/usage data are not available to justify deleting intermediate-term scenarios. Based on use data, HED believes that residential exposures to the JITF inert cluster inert ingredients through applied pesticide formulations may occur over a single day or up to weeks at a time for many use-patterns and that intermittent exposure over several weeks may also occur. Long-term handler exposures are not generally expected to occur for long-term exposure scenarios,

While occupational assessments are typically completed by HED using different levels of risk mitigation, residential handler scenarios are assessed assuming short-sleeve shirts and shorts for the handler.

The exposure assessment team used a rate of 4.5 lbs product/A. This estimate is based on the following assumptions: Five (5) gallons of formulated pesticide solution are assumed to be used per day by a residential handler (Revised Residential SOPs Area Treated, February, 2001). Consistent with the residential SOPs, the density of the formulated pesticide solution is assumed to be 9 lbs/gallon. The product concentrate is assumed to be diluted at a 1 to 10 ratio with water.

5 gallons formulated pesticide solution*(9 lbs/gallon)*(1 part product concentrate/10 parts water) = 4.5 lbs product per day

This application rate of product can be multiplied by the percentage of inert in each product type (herbicide, insecticide or fungicide) to be used as application rates in the risk assessment to account for inert in the product.

E2. Residential Handler/Applicator Exposures

The Agency believes that there are distinct job functions or tasks related to applications and that exposures can vary depending on the specifics of each task. Job requirements (e.g., amount of chemical to be used in an application), the kinds of equipment used, the crop or target being treated, and the circumstances of the user (e.g., the level of protection used by an applicator) can cause exposure levels to differ in a manner specific to each application event.

Exposure Data Sources

The Agency uses exposure scenarios to describe the various types of handler exposures that may occur for a specific active ingredient. The use of scenarios as a basis for exposure assessment is very common as described in the U.S. EPA Guidelines for Exposure Assessment (U.S. EPA; Federal Register Volume 57, Number 104; May 29, 1992). Information from the current labels, use and usage information, toxicology data, and exposure data were all key components in the development of the exposure scenarios. The Agency has developed a series of general descriptions for tasks that are associated with pesticide applications. A residential handler is a term used to describe those individuals who are involved in the pesticide application process. As residential products typically are already mixed, residential handler exposure scenarios are based on application exposure only.

A chemical can produce different effects based on how long a person is exposed, how frequently exposures occur, and the level of exposure. The Agency classifies exposures up to 30 days as short-term and exposures greater than 30 days up to several months as intermediate-term. Based on use data and label instructions, the Agency believes that residential exposures to the JITF inert cluster inert ingredients may occur over a single day or up to 30 days at a time for the use patterns. Long-term handler exposures are not expected to occur for chemicals in the JITF inert cluster inert ingredients cluster.

Other parameters are also defined from use and usage data such as application rates and application frequency. The Agency typically completes exposure assessments using maximum application rates for each scenario to ensure there are no concerns for each specific use.

No chemical-specific handler exposure data were submitted in support of this action to inform daily dose calculations. It is the policy of HED to use data from PHED Version 1.1 as presented in the PHED Surrogate Exposure Guide (8/98) to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available (HED Science Advisory Council for Exposure [ExpoSAC] Draft Policy # 7, dated 1/28/99). Additionally, typical HED standard values were used for the amount treated per day (ExpoSAC Policy # 9, dated 7/5/00).

The residential handler/applicator exposures are calculated using unit exposure data from the Pesticide Handlers Exposure Database (PHED). PHED was designed by a task force of representatives from the US EPA, Health Canada, the California Department of Pesticide Regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts – a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates). The distribution of exposure values for each body part (e.g., chest, upper arm) is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is then selected from the distribution of the exposure values for each body part. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. Once selected, the central tendency values for each body part are composited into a "best fit" exposure value representing the entire body.

The unit exposure values calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based upon the number of observations and the available quality control data. While data from PHED provide the best available information on handler exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposures for many residential scenarios that can be used to ensure consistency in exposure assessments. Unit exposures are used which represent different levels of personal protection as described above. Protection factors were used to calculate unit exposures for varying levels of personal protection if data were not available.

ORETF Handler Studies (MRID 449722-01): A report was submitted by the ORETF (Outdoor Residential Exposure Task Force) that presented data in which the application of various products used on turf by homeowners and lawn care operators (LCOs) was monitored. All of the data submitted in this report were completed in a series of studies. These studies are summarized in the HED Memorandum "Summary of HED's Reviews of ORETF Chemical Handler Exposure Studies: MRID 449722-01", DP Barcode D261948 of April 30, 2001. The studies performed used dacthal as a surrogate compound with a target application rate of 2.0 lbs/ai. All studies were conducted in accordance with current Agency guidelines, have been reviewed by HED and Health Canada, and the data generated were of high quality.

Assumptions for Handler Exposure Scenarios

General assumptions regarding the residential handler scenarios assessed are as follows:

- Residential handler exposure estimates were based on surrogate data from the Pesticide Handlers Exposure Database (PHED, V.1.1, 1998) and Outdoor Residential Exposure Task Force (ORETF) data. Appendix E contains additional information about the data sources used to assess residential exposure.
- HED has developed standard unit exposures for many scenarios to ensure consistency in exposure assessments. These standard values were used to calculate handler exposures for the associated scenarios.
- The adverse effects for the short- and intermediate-term dermal and inhalation endpoints are based on studies where the effects were not gender specific, therefore, the body weight of an average human (70 kg) was used to estimate exposure.
- The daily areas treated were defined for each handler scenario (in appropriate units) by determining the amount that can be reasonably treated by a residential handler in a single day. When possible, the assumptions for daily areas treated are taken from the Health Effects Division Science Advisory Committee on Exposure Policy 9: "Standard Values for Daily Acres Treated in Agriculture".

Residential Handler Exposure and Risk Calculations

Residential Handler Exposure and Risk Calculations

Potential dermal and inhalation daily exposures for occupational handlers were calculated using the following formulas:

Daily Inhalation Exposure (mg inert /day) = UE (µg inert/ lb inert) * CF * AR * AT

Daily Dermal Exposure (mg inert / day) = UE (mg inert / lb inert) * AR * AT

Where:
UE = Unit Exposure (from PHED) (µg or mg inert / lb inert)
CF = conversion factor to convert µg to mg (1 mg /1000 µg)- for inhalation exposure only
AR = application rate (lb inert/ A)
AT = daily acres treated (Acres/day)

The inhalation and dermal daily doses were calculated using the following formulas:

Daily Inhalation Dose (mg /kg/day) = Daily Inhalation Exposure (mg /day) * 1/Body Weight (kg) * 1 (100% Inhalation absorption)

Daily Dermal Dose (mg /kg/day) = Daily Dermal Exposure (mg /day) * 1/Body Weight (kg) * 0.05 (5% Dermal absorption)

Margin of Exposure: Dermal and inhalation risks for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the PoD to the daily dose of concern. All MOE values were calculated for dermal and inhalation exposure levels.

Where:

MOE = PoD (mg/kg/day) / ADD (mg/kg/day)

MOE = Margin of Exposure: value used by HED to represent risk or risk estimates (unitless)
PoD = Point of Departure
NOAEL = No Observed Adverse Effect Level: Dose level in a toxicity study
ADD = Average Daily Dose: the absorbed dose received from exposure to a pesticide in a given scenario

Risk estimates are presented for the route of exposure in each scenario, because risk mitigation measures are specific to the route of exposure.

Total Margins of Exposure: Where appropriate, the endpoint selected for both dermal and inhalation exposure is combined to include both dermal and inhalation routes of exposure using the following equation.

Total MOE = 1/ (1/ Dermal MOE + 1/ Inhalation MOE)

The level of concern for all assessments is established by the uncertainty factor. The level of concern is an MOE of 100 for the JITF inert cluster inert ingredients dermal and inhalation residential exposure scenarios (short- and intermediate-term exposure duration.

E3. Residential Postapplication Exposures

No crop-specific dislodgeable foliar residue (DFR) or transferable turf residue (TTR) data is available for the JITF inert cluster inert ingredients. A default residential postapplication assessment was conducted, including a default 5% of the JITF inert cluster inert ingredients application rate as the initial concentration and a 10% daily dissipation rate. This is adapted from the ExpoSAC SOP No. 003 (May 7th, 1998 - Revised August 7th, 2000).

Assumptions for Handler Exposure Scenarios

General assumptions regarding the residential handler scenarios assessed are as follows:

- The average residential workday is assumed to be 8 hours.
- The adverse effects for the short- and intermediate-term dermal PoDs are based on studies where the effects were observed in both sexes, therefore, the body weight of an average human (70 kg) was used to estimate exposure.
- HED has developed standard transfer coefficient values for residential postapplication scenarios to ensure consistency in exposure assessments. These standard values were used to calculate postapplication exposures.
- No postapplication data were submitted for the inert cluster; a default 5% of the application rate is used in conjunction with 10% default daily dissipation rate.

Residential Postapplication Outdoor Exposure and Risk Calculations

General assumptions regarding the occupational handler scenarios assessed are as follows:

- The adverse effects for the short- and intermediate-term dermal and inhalation endpoints are based on studies where the effects were observed in both sexes, therefore, the body weight of an average human (70 kg) was used to estimate exposure. The body weight of an average child is 15 kg.
- HED has developed standard transfer coefficient values for occupational postapplication scenarios to ensure consistency in exposure assessments.

Potential dermal postapplication exposure was calculated using the following formulas:

Adult and Child Dermal Exposure to Treated Lawns:

$$ADD = \frac{TTR * TC * ET * CF1 * DA}{BW}$$

Where:
ADD= Average Daily Dose (mg/kg/day)
TTR= Turf Transferable Residue ($\mu g/cm^2$)
TC = Transfer Coefficient (cm^2/hr) (14,500 cm^2/hr for adults, 5,200 cm^2/hr for children for short-term exposure durations; and 7,300 cm^2/hr for adults, 2,600 cm^2/hr for children for intermediate-term exposure durations)

ET = Exposure Time (2 hr)
CF1 = Conversion Factor (1 mg / 1000 µg)
DA = Dermal Absorption Factor (5%)
BW = Body Weight (70 kg for adult, 15 kg for child)

$$TTR = AR * (1\text{-}D)^t * F * CF1 * CF2$$

Where:
AR = Application Rate (lb inert/acre)
F = fraction of inert retained on foliage or 5% (unitless)
D = fraction of residue that dissipates daily or 10% (unitless)
t = number of days after application day (Day 0; day of application)
CF1 = 4.54×10^{8} µg/lb
CF2 = 24.7×10^{-9} acre/cm^2

Hand to Mouth Exposure to Child on Treated Turf (from SOP 2.3.2):

The following equation is used to calculate the nondietary ingestion exposures that are attributable to hand-to-mouth behavior on treated turf:

$$ADD = \frac{TTR * SA * SE * Freq * CF1 * ET}{BW}$$

Where:
ADD = Average daily dose (mg/kg/day)
TTR= turf transferable residue (µg/cm^2)
SA= Surface area of child hand- 3 fingers (20 cm^2/event)
SE = Saliva Extraction Factor (0.5)
Freq = Frequency of hand-to-mouth events (20 events/hr for short-term exposures, 9.5 events/hr for long-term exposures)
CF1 = 1 mg/ 1000 µg
ET = Exposure Time (2 hours)
BW = Body weight (15 kg for child)

$$TTR = AR * (1\text{-}D)^t * F * CF1 * CF2$$

Where:
AR = Application Rate (lb inert/acre)
F = fraction of inert retained on foliage/surface or 5% (unitless)
D = fraction of residue that dissipates daily or 10% (unitless)
t = number of days after application day (0 days); day of application
CF1 = 4.54×10^{8} µg/lb
CF2 = 24.7×10^{-9} acre/cm^2

Object to Mouth Exposure to Child:

The following equation is used to calculate the nondietary ingestion exposures that are attributable to object-to-mouth behavior on treated turf:

$$ADD = \frac{TTR * IgR * CF1}{BW}$$

Where:
TTR = object transferable residue (µg/cm^2)
IgR = Ingestion Rate for mouthing per day (25 cm^2/day)
CF1 = 1 mg / 1000 µg
BW = Body weight (15 kg for child)

$$TTR = AR * (1\text{-}D)^t * F * CF1 * CF2$$

Where:
AR = Application Rate (lb inert/acre)
F = fraction of inert retained on object or 20% (unitless)
D = fraction of residue that dissipates daily or 10% (unitless)
t = number of days after application day (0 days); day of application
CF1 = 4.54 x 10^8 µg/lb
CF2 = 24.7 x 10^{-9} acre/cm^2

Soil Ingestion Exposure to Child:

The following equation is used to calculate the nondietary ingestion exposures that are attributable to soil ingestion on treated turf:

$$ADD = \frac{SR * IgR * CF1}{BW}$$

Where:
ADD = Average daily dose (mg/kg/day)
SR = Soil Residue, 1 cm depth of surface soil, (µg/g)
IgR = Ingestion Rate for daily soil ingestion (100 mg/day)
CF1 = Conversion Factor (1 g / 1,000,000 µg)
BW = Body weight (15 kg for child)

$$\text{Soil Residue (SR)} = AR * CF1 * CF2 * CF3 * F * (1\text{-}D)^t$$

Where:
AR= application rate (lb inert/ A)
CF1 = 4.54 x 10^{8} µg/lb
CF2 = 24.7 x 10^{-9} acre/cm^2
CF3 = Conversion factor (0.67 cm^3 / g soil)
F = fraction of inert retained on soil or 100% (unitless)
D = fraction of residue that dissipates daily (unitless)
t = postapplication day on which exposure is being assessed (t = 0, day of application)

The Aggregate Risk for inert cluster is calculated for residential postapplication by adding the daily doses for child dermal exposure to lawns and child hand-to-mouth exposure to treated lawns. This method is used because the PoD is the same for both of the above scenarios. Then, the risk estimate is calculated by dividing the PoD by the combined daily dose.

Assumptions for Dermal Dose from Pesticide Residues on Turf:

- On the day of application, it may be assumed that 5% of the application rate are available from the turfgrass as dislodgeable residue.
- Postapplication is assessed on the same day the pesticide is applied because it is assumed that the homeowner could be exposed to turfgrass immediately after application. Therefore, postapplication exposures are based on day 0 (i.e., the day of application).
- The upper percentile dermal transfer coefficient is assumed to be 14,500 cm^2/hr for adults and 5,200 cm^2/hr for children for short-term durations; and 7,300 cm^2/hr for adults and 2,600 cm^2/hr for children for intermediate-term durations. The transfer coefficient cm^2/hr is a calculated mean, based on the Jazzercise method, which is believed to result in an upper percentile estimate of the transfer coefficient for this scenario.
- The duration of exposure for children and adults is assumed to be 2 hours per day. The 95th percentile value for playing on grass is 121 minutes per day for both age groups 1-4 years and 18-64 years (U.S. EPA 1996).

Assumptions for Potential Dose among children from Incidental Nondietary Ingestion of Pesticide Residues on Residential Lawns from Hand-to-Mouth Transfer:

- On the day of application, it may be assumed that 5% of the application rate is available on the turfgrass as dislodgeable residue.
- Postapplication activities are assessed on the same day that the pesticide is applied because it is assumed that children could play on the lawn immediately after application.
- The surface portion of three fingers of a toddler's hand put in mouth is 20 cm^2.
- The Hand-to-Mouth (HTM) exposure frequency is 20 times per hour for short term exposures.
- The HTM exposure frequency is 9.5 times per hour for intermediate term exposures.

- The duration of exposure for toddlers is assumed to be 2 hours per day. The 95th percentile value for playing on grass is 121 minutes per day for both age groups 1-4 years and 18-64 years (U.S. EPA 1996).
- Toddlers (age 3 years), used to represent the 1 to 6 year old age group, are assumed to weigh 15 kg. (U.S. EPA 1996).
- The saliva extraction factor is 50%.

Assumptions for Potential Dose among Toddlers from the Ingestion of Pesticide-Treated Turfgrass:

- On the day of application, it may be assumed that 20% of the application rate is available on the turfgrass as dislodgeable residue.
- Postapplication activities are assessed on the same day that the pesticide is applied because it is assumed that children could play on the lawn immediately after application.
- The assumed ingestion rate for grass for toddlers (age 3 years) is 25 cm^2/day. This value is intended to represent the approximate area from which a child may grasp a handful of grass.

Assumptions for Potential Dose among Toddlers from Incidental Ingestion of Soil from Pesticide-Treated Residential Areas:

- On the day of application, it is assumed 100% of the application rate is located within the soil's uppermost 1 cm.
- Postapplication must be assessed on the same day the pesticide is applied because it is assumed that toddlers could play on the lawn or other outdoor treated areas immediately after application.
- The assumed soil ingestion rate for children (age 1-6 years) is 100 mg/day (U.S. EPA 1996).

References

(A) PHED Surrogate Exposure Guide, V1.1. Health Effects Division, Office of Pesticide Program. August, 1998.

(B) Series 875 - Occupational and Residential Exposure Test Guidelines, Group B - Post Application Exposure Monitoring Test Guidelines. U.S. EPA. February 10, 1998.

APPENDIX F

F.1. Occupational Exposure Assessment Introduction

This document is a summary of the methods used to calculate occupational exposures to the inert cluster inert ingredients. These methods and a basic description of how they are used were taken from References A and B. These references also contain more detailed information on the rationale behind these methods. Only those methods pertinent to the JITF inert cluster inert ingredients exposures are discussed in this document.

Tasks associated with occupational pesticide handlers are categorized using one of the following terms:

- Mixers and/or Loaders: these individuals perform tasks in preparation for an application. For example, mixers/loaders would mix and prepare the product prior to application.
- Mixer/Loader/Applicators and or Loader/Applicators: these individuals are involved in the entire pesticide application process (they do all job functions related to a pesticide application event). These individuals would perform the mix/load function, transfer the product (containing the inert) into the application equipment, and then complete the product application.

A chemical can produce different effects based on how long a person is exposed, how frequently exposures occur, and the level of exposure. HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. HED completes both short- and intermediate-term assessments for occupational scenarios in all cases because these kinds of exposures are likely and acceptable use/usage data are not available to justify deleting intermediate-term scenarios. Based on use data, HED believes that occupational exposures to the JITF inert cluster inert ingredients may occur over a single day or up to weeks at a time for many use-patterns and that intermittent exposure over several weeks may also occur. Some applicators may apply the products containing inerts over a period of weeks, because they are commercial applicators who are completing multiple applications for multiple clients. Long-term handler exposures can occur in ornamental treatment scenarios, where handlers can apply pesticides all year long in greenhouses and hothouses.

Usually occupational handler exposure assessments are completed by HED using different levels of risk mitigation. Typically, HED uses a tiered approach. The lowest tier is designed as the baseline exposure scenario (i.e. long-sleeve shirt, long pants, shoes, socks, no respirator). If risks are of concern at the baseline exposure scenario, then increasing levels of PPE (i.e. gloves, respirators) are evaluated. If risk remains a concern with maximum PPE, then engineering controls (i.e. enclosed cabs or cockpits, water-soluble packaging, and closed mixing/loading systems) are evaluated. This approach is used to ensure that the lowest level of risk mitigation that provides adequate protection is selected, since the addition of PPE and engineering controls involves an additional expense to the user and (in the case of PPE) also involves an additional

burden to the user due to decreased comfort and dexterity and increased heat stress and respiratory stress.

F2. Occupational Handler/Applicator Exposures

The Agency believes that there are distinct job functions or tasks related to applications and that exposures can vary depending on the specifics of each task. Job requirements (e.g., amount of chemical to be used in an application), the kinds of equipment used, the crop or target being treated, and the circumstances of the user (e.g., the level of protection used by an applicator) can cause exposure levels to differ in a manner specific to each application event.

Exposure Data Sources

The Agency uses exposure scenarios to describe the various types of handler exposures that may occur for a specific active ingredient. The use of scenarios as a basis for exposure assessment is very common as described in the U.S. EPA Guidelines for Exposure Assessment (U.S. EPA; Federal Register Volume 57, Number 104; May 29, 1992). Information from the current labels, use and usage information, toxicology data, and exposure data were all key components in the development of the exposure scenarios. The Agency has developed a series of general descriptions for tasks that are associated with pesticide applications. Tasks associated with occupational pesticide handlers are categorized using one of the following terms:

- Mixers and/or Loaders: These individuals perform tasks in preparation for an application. For example, prior to application, mixer/loaders would mix the JITF inert cluster inert ingredients and load them into the holding tank of the groundboom.

- Applicators: These individuals operate application equipment during the release of a pesticide product into the environment. These individuals can make applications using equipment such as groundboom.

- Mixer/Loader/Applicators and or Loader/Applicators: These individuals are involved in the entire pesticide application process (i.e., they do all job functions related to a pesticide application event). These individuals would transfer the JITF inert cluster inert ingredients into the application equipment and then also apply it.

A chemical can produce different effects based on how long a person is exposed, how frequently exposures occur, and the level of exposure. The Agency classifies exposures up to 30 days as short-term and exposures greater than 30 days up to several months as intermediate-term. Based on use data and label instructions, the Agency believes that occupational the JITF inert cluster inert ingredients exposures may occur over a single day or up to 30 days at a time for the use patterns. Long-term handler exposures are not expected to occur for the JITF inert cluster inert ingredients.

Other parameters are also defined from use and usage data such as application rates and application frequency. The Agency typically completes exposure assessments using maximum application rates for each scenario to ensure there are no concerns for each specific use.

Occupational handler exposure assessments are completed by the Agency using different levels of risk mitigation. Typically, the Agency uses a tiered approach. The lowest tier is designated as the baseline exposure scenario (i.e., no respirator). If risks are of concern at baseline attire, then increasing levels of personal protective equipment or PPE (e.g., respirators) are evaluated. If risks remain of concern with maximum PPE, then engineering controls (e.g., enclosed cabs, water-soluble packaging, and closed mixing/loading systems) are evaluated. This approach is used to ensure that the lowest level of risk mitigation that provides adequate protection is selected, since the addition of PPE and engineering controls involves an additional expense to the user. PPE also involves an additional burden to the user due to decreased comfort and dexterity and increased heat stress and respiratory stress.

No chemical-specific handler exposure data were submitted in support of this action to inform daily dose calculations. It is the policy of HED to use data from PHED Version 1.1 as presented in the PHED Surrogate Exposure Guide (8/98) to assess handler exposures for regulatory actions when chemical-specific monitoring data are not available (HED Science Advisory Council for Exposure [ExpoSAC] Draft Policy # 7, dated 1/28/99). Additionally, typical HED standard values were used for the amount treated per day (ExpoSAC Policy # 9, dated 7/5/00).

The occupational handler/applicator exposures are calculated using unit exposure data from the Pesticide Handlers Exposure Database (PHED). PHED was designed by a task force of representatives from the US EPA, Health Canada, the California Department of Pesticide Regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts – a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to subset and statistically summarize the selected data. Currently, the database contains values for over 1,700 monitored individuals (i.e., replicates). The distribution of exposure values for each body part (e.g., chest, upper arm) is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is then selected from the distribution of the exposure values for each body part. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. Once selected, the central tendency values for each body part are composited into a "best fit" exposure value representing the entire body.

The unit exposure values calculated by PHED generally range from the geometric mean to the median of the selected data set. To add consistency and quality control to the values produced from this system, the PHED Task Force has evaluated all data within the system and has developed a set of grading criteria to characterize the quality of the original study data. The assessment of data quality is based upon the number of observations and the available quality control data. While data from PHED provide the best available information on handler

exposures, it should be noted that some aspects of the included studies (e.g., duration, acres treated, pounds of active ingredient handled) may not accurately represent labeled uses in all cases. HED has developed a series of tables of standard unit exposures for many occupational scenarios that can be used to ensure consistency in exposure assessments. Unit exposures are used which represent different levels of personal protection as described above. Protection factors were used to calculate unit exposures for varying levels of personal protection if data were not available.

ORETF Handler Studies (MRID 449722-01): A report was submitted by the ORETF (Outdoor Residential Exposure Task Force) that presented data in which the application of various products used on turf by homeowners and lawn care operators (LCOs) was monitored. All of the data submitted in this report were completed in a series of studies. These studies are summarized in the HED Memorandum "Summary of HED's Reviews of ORETF Chemical Handler Exposure Studies: MRID 449722-01", DP Barcode D261948 of April 30, 2001. The studies performed used dacthal as a surrogate compound with a target application rate of 2.0 lbs/ai. All studies were conducted in accordance with current Agency guidelines, have been reviewed by HED and Health Canada, and the data generated were of high quality.

Assumptions for Handler Exposure Scenarios

General assumptions regarding the occupational handler scenarios assessed are as follows:

- Occupational handler exposure estimates were based on surrogate data from the Pesticide Handlers Exposure Database (PHED, V.1.1, 1998)
- HED has developed standard unit exposures for many occupational scenarios to ensure consistency in exposure assessments. These standard values were used to calculate handler exposures for the associated scenarios.
- The adverse effects for the short- and intermediate-term dermal and inhalation endpoints are based on studies where the effects were not gender specific, therefore, the average adult body weight representing the general U.S. population (70 kg) was used.
- The daily areas treated were defined for each handler scenario by determining the amount that can be reasonably treated in a single day. The assumptions for daily areas treated are taken from the Health Effects Division Science Advisory Committee on Exposure Policy 9: "Standard Values for Daily Acres Treated in Agriculture".

Table F2: Occupational Handler Dermal and Inhalation Unit Exposures used for Occupational Handler Assessments

Exposure Scenario*	Dermal Unit Exposure (mg/ lb ai)				Inhalation Unit Exposure (µg/ lb ai)			
	Baseline	Baseline + Gloves	Max PPE	Eng. Control	Baseline	Baseline + Gloves	Max PPE	Eng. Control
Mixer/Loader Scenarios								
Liquids/ Aerial Application/ High Acreage Crops	2.9	0.023	0.017	0.0086	1.2	0.24	0.12	0.083
Liquids/ Airblast/ Nut Tree								
Liquids/ Groundboom/ High Acreage Crops								
Liquids/ Groundboom/ Turf								
Liquids/ Low Pressure Handwand/ Turf								
Wettable Powder/ Airblast/ Nut Tree	3.7	0.17	0.13	0.0098	43	8.6	4.3	0.24
Wettable Powder/ Groundboom/ High Acreage Crops								
Wettable Powder/ Groundboom/ Turf								
Wettable powder/ Low Pressure Handwand/ Turf								
Applicator Scenarios								
Liquid/ Aerial Application/ High Acreage Crops	NA	NA	NA	0.0055	NA	NA	NA	0.068
Airblast/ Nut Tree	0.36	0.24	0.13	0.019	4.5	0.9	0.45	0.09
Groundboom/ High Acreage Crops	0.014	0.014	0.011	0.0051	0.74	0.148	0.074	0.043
Groundboom/ Turf								
Mixer/Loader/Applicator Scenarios								
Low Pressure Handwand/ Turf (ORETF data)	NA	0.65	0.36	NA	6.6	1.32	0.66	NA
Wettable Powder/ Low Pressure Handwand/ Ornamentals	NA	8.6	6.2	NA	1100	220	110	NA
Liquid/ Low Pressure Handwand/ Ornamentals	100	0.43	0.37	NA	30	6	3	NA
Flagger Scenarios								
Liquid/ Flagger/ High Acreage Crops	0.011	0.012	0.011	0.0022	0.35	0.07	0.035	0.007

Values are reported in the PHED Surrogate Exposure Guide dated August 1998.

APPLICATION RATES USED FOR THE JITF INERT INGREDIENTS RISK ASSESSMENT

Table F3: Application Rates* used for Occupational Handler Exposure Assessment			
Exposure Scenario (Formulation/ Application/ Crop)	Product Type	Short-Term (Maximum Rate)	Intermediate-term (Average Rate)
Mixer/Loader Scenarios			
Liquids/ Aerial Application/ High Acreage Crops	Herbicide	10.4	2
	Insecticide	2	0.7
	Fungicide	5	0.7
Liquids/ Airblast/ Nut Tree	Herbicide	7.2	3.2
	Insecticide	9	2.5
	Fungicide	11	3
Liquids/ Groundboom/ High Acreage Crops	Herbicide	10.4	2
	Insecticide	2	0.7
	Fungicide	5	0.7
Liquids/ Groundboom/ Turf	Herbicide	10.4	2
	Insecticide	2	0.7
	Fungicide	5	0.7
Liquids/ Low Pressure Handwand/ Turf	Herbicide	7.2	7.2
	Insecticide		
	Fungicide		
Wettable Powder/ Airblast/ Nut Tree	Herbicide	1.6	1.6
	Insecticide	6	3
	Fungicide	7	2
Wettable Powder/ Groundboom/ High Acreage Crops	Herbicide	1.6	1
	Insecticide	1.6	0.7
	Fungicide	1	0.6
Wettable Powder/ Groundboom/ Turf	Herbicide	1.6	1
	Insecticide	1.6	0.7
	Fungicide	1	0.6
Wettable powder/ Low Pressure Handwand/ Turf	Herbicide	7.2	7.2
	Insecticide		
	Fungicide		
Applicator Scenarios			
Liquid/ Aerial Application/ High Acreage Crops	Herbicide	10.4	2
	Insecticide	2	0.7
	Fungicide	5	0.7
Airblast/ Nut Tree	Herbicide	1.6	1.6
	Insecticide	9	2.5
	Fungicide	7	3
Groundboom/ High Acreage Crops	Herbicide	10.4	2
	Insecticide	2	0.7
	Fungicide	5	0.7

Table F3: Application Rates* used for Occupational Handler Exposure Assessment			
Exposure Scenario (Formulation/ Application/ Crop)	Product Type	Short-Term (Maximum Rate)	Intermediate-term (Average Rate)
Groundboom/ Turf	Herbicide	10.4	2
	Insecticide	2	0.7
	Fungicide	5	0.7
Mixer/Loader/ Applicator Scenarios			
Low Pressure Handwand/ Turf (ORETF data)	Herbicide	7.2	7.2
	Insecticide		
	Fungicide		
Wettable Powder/ Low Pressure Handwand/ Ornamentals	Herbicide		
	Insecticide		
	Fungicide		
Liquid/ Low Pressure Handwand/ Ornamentals	Herbicide		
	Insecticide		
	Fungicide		
Flagger Scenarios			
Liquid/ Flagger/ High Acreage Crops	Herbicide	10.4	2
	Insecticide	2	0.7
	Fungicide	5	0.7

* Application rates are multiplied by the percentage of inert in each product type when used as application rates in the risk assessment.

Occupational Handler Exposure and Risk Calculations

Daily Exposure: Daily inhalation handler exposure is estimated for each applicable handler task with the application rate, the amount handled in a day, and the applicable inhalation unit exposure using the following formula:

*Daily Exposure (mg ai/day) = Unit Exposure (mg ai/lb ai handled) * Application Rate (lbs ai/gal) * Daily Area Treated (gal/day)*

Where:

Daily Exposure	=	Amount (mg or µg ai/day) inhaled that is available for inhalation absorption;
Unit Exposure	=	Unit exposure value (mg or µg ai/day) derived from August 1998 PHED data;
Application Rate	=	Normalized application rate based on a logical unit treatment, such as gallons. Maximum values are generally used (lb ai/gal); and
Daily Area Treated	=	Normalized application area based on a logical unit treatment such as gallons per day (gal/day).

Daily Dose: The daily inhalation dose is calculated by normalizing the daily exposure by body weight and adjusting, if necessary, with an appropriate inhalation absorption factor. For all inhalation exposure scenarios for the JITF inert cluster inert ingredients, an average adult body weight of 70 kilograms was used. For inhalation exposures, an absorption factor of 100% was assumed.

Daily dose was calculated using the following formula:

*Average Daily Dose (mg/kg/day = (Daily Exposure (mg ai/day) * (Absorption Factor (100%) / Body Weight (kg)*

Where:

Average Daily Dose	=	Absorbed dose received from exposure to a pesticide in a given scenario (mg pesticide active ingredient/kg body weight/day);
Daily Exposure	=	Amount (mg ai/day) inhaled that is available for inhalation absorption;
Absorption Factor	=	A measure of the amount of chemical that crosses a biological boundary such as the lungs (% of the total available absorbed); and
Body Weight	=	Body weight determined to represent the population of interest in a risk assessment (kg).

Margins of Exposure: Noncancer inhalation risks for each applicable handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the daily dose to the toxicological endpoint of concern. All MOE values were calculated inhalation exposure levels using the formula below:

MOE = (NOAEL (mg/kg/day) / Average Daily Dose (mg/kg/day)

Where:

MOE	=	Margin of Exposure, value used by HED to represent risk or how close a chemical exposure is to being a concern (unitless);
ADD	=	Average Daily Dose or the absorbed dose received from exposure to a pesticide in a given scenario (mg pesticide active ingredient/kg body weight/day); and
NOAEL	=	Dose level in a toxicity study, where no observed adverse effects (NOAEL) occurred in the study

The level of concern for all assessments is established by the uncertainty factor. The uncertainty factor is 100 for the JITF inert cluster inert ingredients inhalation occupational exposure scenarios for all exposure durations.

Total Margins of Exposure: Where appropriate, the endpoint selected for both dermal and inhalation exposure is combined to include both dermal and inhalation routes of exposure using the following equation.

Total MOE = 1/ (1/ Dermal MOE + 1/ Inhalation MOE)

F3. Occupational Postapplication Exposures

No crop-specific dislodgeable foliar residue (DFR) or transferable turf residue (TTR) data is available for the JITF inert cluster inert ingredients. A default occupational postapplication assessment was conducted, including a default 20% of the JITF inert cluster inert ingredients application rate as the initial concentration and a 10% daily dissipation rate. This is adapted from the ExpoSAC SOP No. 003 (May 7th, 1998 - Revised August 7th, 2000).

Assumptions for Handler Exposure Scenarios

General assumptions regarding the occupational handler scenarios assessed are as follows:

- The average occupational workday is assumed to be 8 hours.
- The adverse effects for the short- and intermediate-term dermal PoDs are based on studies where the effects were observed in both sexes, therefore, the body weight of an average human (70 kg) was used to estimate exposure.
- HED has developed standard transfer coefficient values for occupational postapplication scenarios to ensure consistency in exposure assessments. These standard values were used to calculate postapplication exposures.
- No postapplication data were submitted for the JITF inert cluster inert ingredients; a default 20% of the application rate for foliar crop or 5% of the application rate for turf is used in conjunction with 10% default daily dissipation rate.

Because the postappplication assessment was conducted for a few specific crop groups with high exposure worker reentry activity patterns, HED customized the JITF inert cluster inert ingredient application rate for the three postapplication crop groupings (corn/grapes/turf & sod). See Table 3 below.

Table 3: Application Rates used for Occupational Postapplication Scenarios

Crop	Product Type	Short-Term (Maximum Rate)	Intermediate-term (Average Rate)
Corn	Herbicide	10.4	1.2
	Insecticide	10	1
	Fungicide	5	1
Grapes	Herbicide	4.8	2.28
	Insecticide	7	3
	Fungicide	5	2
Turf/Sod	Herbicide	10.4	1.2
	Insecticide	10	1
	Fungicide	5	1

* Application rates are multiplied by the percentage of inert in each product type when used as application rates in the risk assessment to account for inert in the product.

Occupational Postapplication Exposure and Risk Calculations

Potential dermal postapplication exposure was calculated using the following formulas (Appropriate dermal absorption used):

$$\text{Dislodgable Foliar Residue } (\mu g/cm^2) = AR * F * (1\text{-}D)^t * CF1 * CF2$$

Where:
AR = Application Rate (lb inert/acre)
F = fraction of ai retained on foliage or 20% for foliar crop or 5% for turf (unitless)
D = fraction of residue that dissipates daily or 10% (unitless)
t = number of days after application day (days)
CF1 = 4.54×10^{8} µg/lb
CF2 = 24.7×10^{-9} acre/cm^2

$$\text{Daily Dermal Dose (mg/kg/day)} = \frac{DFR_t * CF3 * Tc * DA * ET}{BW \text{ (kg)}}$$

Where:
DFRt = dislodgable foliar residue on day "t" (µg/cm^2)
CF3 = 1×10^{-3} mg/µg
Tc = transfer coefficient (cm^2/hr)
DA = dermal absorption factor (unitless)
ET = exposure time (hr/day)
BW = body weight (kg)

Margin of Exposure: Dermal risks for the postapplication scenarios are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological point of departure to the daily dose of concern.

$$MOE = \text{PoD (typically a NOAEL in mg/kg/day)} / \text{ADD (mg/kg/day)}$$

Where:
MOE = Margin of Exposure: value used by HED to represent risk or risk estimates (unitless)
Po D = Point of Departure
NOAEL = No Observed Adverse Effect Level: Dose level in a toxicity study
ADD = Average Daily Dose: the absorbed dose received from exposure to a pesticide in a given scenario

References

(B) PHED Surrogate Exposure Guide, V1.1. Health Effects Division, Office of Pesticide Program. August, 1998.

(C) Series 875 - Occupational and Residential Exposure Test Guidelines, Group B - Post Application Exposure Monitoring Test Guidelines. U.S. EPA. February 10, 1998.